A STUDY OF THE AUDITORY CORTEX IN THE GUINEA PIG WITH IMPLICATIONS FOR THE DEVELOPMENT OF AN ELECTRICAL PROSTHESIS FOR THE HARD OF HEARING

by

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INTRODUCTION

The ultimate goal of this investigation is to provide information that would be helpful in developing a device to electrically stimulate the human auditory nerve. Such a device could be used in cases of sensorineural hearing loss. At this time, a number of attempts to use such an electrical prosthesis clinically have been tried. A study by Blair Simmons (1964) was one of the most successful of these attempts.

In that study, Simmons was able to stimulate the auditory nerve and the inferior colliculus of a young man undergoing surgery for the removal of a tumor. Since the patient was under a local anesthetic, he was able to report his perception of the electrical stimulus. Square pulses were used. Below the stimulation rate of 1,000 pulses per second, changes in the rate of stimulation were reported as changes in pitch. Very good correspondence between pitch and rate of stimulation was obtained. The differential threshold was about 5 pulses per second. Between 1,000 and 3,000 cycles per second, the perception of pitch became somewhat confused. When the two electrical stimuli followed one another, the patient could tell which was the higher frequency stimulus. However, if a silent period elapsed between the two electrical stimuli, the patients ability to discriminate the two rates was severely impaired. Above 3,000 cycles per second, the patient could not discriminate rates of stimulation.

In another study, Simmons (1965, 1966) chronically implanted electrodes in a patient. Although the patient was very cooperative, he suffered from tunnel vision and was almost completely deaf.

Moreover, the patient did not understand the concept of pitch at the start of the experiment. Because of these limitations in communication, one cannot be completely confident with the results of the study. Six electrodes had been implanted in the modiolar portion of the eighth nerve. With high rates of stimulation, each electrode seemed to produce a characteristic pitch. With lower rates of stimulation, pitch seemed to be related to the rate of stimulation and was independent of the electrode used.

More recently, House (1970) reported the results obtained from several patients. These patients were totally deaf. He placed a number of stimulating electrodes into the basal 3/4 turn of the cochlea. These electrodes were inserted through the round window. The patients perceived the electrical stimuli, but the qualities of the perception were unclear. Pure tones were not perceived and the prosthesis did not allow speech to be understood.

Michelson (1970) has also reported the clinical use of implanted electrodes. His patients had severe hearing losses. A polyethylene tube containing several electrodes was introduced into the cochlea through the round window. The electrodes consisted of two rail-like strips which would stimulate large portions of the cochlea. Again, electrical stimuli were perceived but the quality of the perception was not clear. Speech was not understood.

These experiments, along with others, were discussed at a

recent meeting held at Stanford Medical School (see House 1970). The conference dealt with implantable prosthesis for hearing. This conference and the experiments cited demonstrate the current interest in the development of electrical prosthesis for the hard of hearing.

At the present time, however, little knowledge exists to guide the surgeon in his implantation of electrical prosthesis. Not even a rough estimation of the current or voltage levels needed to stimulate the auditory nerve are available. Questions about the best positions for the stimulating electrodes or the most efficient stimulus waveform have not been asked. If these problems were solved by animal studies,the surgeon would have a guide in his attempts at clinically implanting an electrical prosthesis.

A few animal studies deal with electrical stimulation of auditory structures. In a study by Neider and Neff (1961), ten cats were prepared with bipolar electrodes chronically implanted in subcortical locations. While four of these cats were trained initially to avoid shock using an acoustical stimulus as a CS, six animals were trained initially using an electrical stimulus as the CS. After initial training, transfer to the other warning stimulus was tested.

All animals initially trained with an acoustical CS, showed immediate transfer to electrical stimulation of the inferior colliculus. On the other hand, stimulation of the cochlear nucleus produced poor results. Transfer effects did not occur or these

effects extinguished early. Electrical stimulation of the cochlear nucleus produced motor responses.

Transfer effects from electrical stimulation to acoustical stimulation were poor. Of the six cats who were trained initially to a electrical CS, three had electrodes in the inferior colliculus. Only one of these three cats showed transfer to an acoustical stimulus. One cat, whose electrodes were in the auditory radiations, responded to clicks but not to pure tones. A cat with an electrode in the medial geniculate responded to only one acoustic stimulus in nine trials. The final cat had electrodes in the optic tract.

Gerken (1966) behaviorally tested the effects of electrically stimulating the inferior and superior colliculi in six guinea pigs. The threshold for a response to a 100 Hz stimulus was about 10 uA. Transfer effects to acoustical stimuli were not tested.

In a more recent study, Gerken (1970) trained cats to respond to electrical stimuli delivered to the cochlear nucleus, the superior olivary complex, the inferior colliculus or the medial geniculate. Gerken found that the more peripheral the stimulation site, the lower the detection threshold. At the cochlear nucleus, the thresholds were between 10 and 75 uA. At the medial geniculate the thresholds were between 150 and 300 uA. Transfer to acoustical stimuli was not tested. However, electrical stimulation through one electrode could be masked by an acoustical stimulus. Masking was attempted in 13 electrode positions; 12 were unsuccessful.

These data indicate that an animal can learn to respond to an electrical stimulus delivered to a subcortical site. However, transfer of this response to an acoustical stimulus seems tenuous.

In the behavioral studies cited, no controls against sensitization were employed. The lack of a sensitization control is not crucial during original training since a sensitization response would still indicate that the animal perceived the stimulus. However, a sensitization control during transfer testing is essential. If sensitization had occurred, the animal might respond to any stimulus. Therefore, a positive transfer effect would not indicate that the two stimuli produced the same percept.

Saunders and Vernon (private communication) at Princeton made a similar attempt using the cat. They had trained the cat to respond to sound. Using a round window electrode, they attempted to electrically stimulate the cochlea. The results of the study were disappointing. The cat responded only to square waves and little information about the quality of the cat's perception was obtained.

Clark (1969), in attempting to gain similar evidence, electrically stimulated the auditory nerve in the cat. By recording unit activity from the contralateral trapezoid body, Clark attempted to compare the effects of acoustical and electrical stimulation. With acoustical stimulation, units in the trapezoid body had best frequencies between 300 and 15K Hz. However, electrical stimuli of similar frequencies could not excite these same units. In fact,

no electrical stimulus above 200 Hz was effective in evoking a response in the trapezoid body.

Clark also attempted to stimulate the cochlea electrically. The stimulus was applied through either bipolar or monopolar round window electrodes. Stimulation of the cochlea also proved to be ineffective in producing a response in the trapezoid body.

In the present dissertation, several problems related to the implantation of an electronic prosthetic device have been investigated. While some of these problems are directly related to the goal, others are tangentally related. As in Clark's study, the original plan of this experiment was to use a neurophysiological response to compare acoustical and electrical stimulation of the ear. The evoked potential of the cerebral cortex was chosen as the neurophysiological response and the guinea pig was chosen as the experimental animal.

The guinea pig was chosen because of his low cost, easy handling and the accessability to the cochlea. The evoked potential of the cerebral cortex was chosen for three reasons. First, the cortex is easy to expose and the evoked potential can be readily recorded. Second, by choosing the cerebral cortex, the largest delay between the stimulus and response was obtained. Since a large electrical artifact was expected at least under some stimulus conditions, the 9 msec latency of the evoked potential was felt to be an asset in separating the response from the stimulus artifact. Finally, by stimulating at the cochlea and recording at the cortex, the entire auditory system is bracketed.

To my knowledge, in only one study (Kayrers and Legouix, 1963) was the auditory cortex of the guinea pig mapped. The animals in that study were anesthetized with sodium pentobarbital and their heads were fixed in a stereotaxic instrument. A silver ball electrode (diameter 1 mm) was employed to monopolarly record the evoked potentials. An indifferent electrode, consisting of a cotton which was soaked in Ringer's solution, was placed in the frontal sinus.

The apparatus that was used to produce the acoustic stimulus was not described in detail. In addition, only three frequencies were employed, 300, 2K, and 15K Hz. The rise time of these tones was 100 msec. and the authors found the onset to be free of transients.

The actual procedure that was used to map the auditory cortex was carefully described. At each of the three frequencies studied, a clearly suprathreshold stimulus was given. The electrode was then moved until it was over an area from which an evoked potential of maximal amplitude was recorded. With the electrode at this point, the intensity of the stimulus was reduced to a point that was just above the threshold for the evoked potential. Then the monopolar electrode was systematically moved across the cortex. In this manner, the extent of the area responding to the just-supraliminal sound was mapped.

Using these methods, Kayrers and Legouix found evidence for two tonotopically organized areas. While one of these areas had responded to all three frequencies, the other area responded to only the low and moderate frequencies. These two areas were separated by a cortical region which had a high threshold and showed no sign of being tonotopically organized. Finally, a posteromedial region was found in which

the evoked potential had an atypical wave form.

Close inspection of the data from the Kayrers and Legouix' study indicated that their map of the auditory cortex was probably correct but not complete. Particularly, the observation of a partial tonotopic area is questionable. Restriction of the stimulus to three frequencies may have obscured part of that area.

The partial tonotopic area found in Kayrers and Legouix study of the guinea pig is similar to some of Woolsey's work on the cat. When Downman, Woolsey and Lende (1960) separated the cortical area Ep from AII, only the basal portion of the cochlea appeared to be represented in Ep. In a later study, Sindberg and Thompson (1962) found that Ep also had an apical representation. Similarly, future studies could be expected to show that both cortical areas in the guinea pig have complete tonotopic representations.

A second lesson from Woolsey's work on the cat might be applicable to the guinea pig. In the pioneering study of Woolsey and Walzl (1942) AII was not clearly differentiated from Ep. These two areas were not clear from the data because the posterior ectosylvian sulcus obscured some of the evoked potentials in most animals. Therefore, Woolsey and Walzl interpreted their data as indicating only two auditory areas, AI and AII.

Woolsey was aware that his evoked potential data was in conflict with the cytoarchitecture studies of Rose (1949a, 1949b). Rose found evidence that caused him to believe that the auditory region of the cat consisted of a central area surrounded by a peripheral belt.

These conclusions were drawn from the changes Rose observed in the layers of cortical cells.

This conflict in results was caused by the anatomical variability within the auditory region. In some animals, the basal portion of AII appeared ahead of the posterior ectosylvian sulcus. The area Ep, in many of these animals, was buried within the depths of the sulcus. In other animals, Ep was clearly located behind the posterior ectosylvian sulcus, but the basal portion of AII was hidden. Each study, however, contained a few individuals in which both areas were visible. After a number of these studies, Woolsey realized that two areas actually existed. Once this insight had been achieved, Woolsey (1960) was able to go back to the record of his earlier studies and find evidence for the existence of AII and Ep. This insight, of course, greatly reduced the conflict between the histological and neurophysiological data.

In the guinea pig, Kayrers and Legouix have indicated the existence of two tonotopic areas. Woolsey and Walzl found two tonotopic areas in the cat. Later work in Woolsey's laboratory indicated that one of those original areas should be further divided. In an analogous fashion, the existence of a third auditory area in the guinea pig would not be surprising.

With this amount of information in the literature, two alternatives could have been pursued in the present project. As one possibility, the data of Kayrers and Legouix could have been quickly checked. Upon finding that their data were generally correct, other studies more

directly pertinent to the electrical prosthetic device could be undertaken. Kern, Cody and Bickford (1969a, 1969b) employed this approach when investigating the averaged cortex evoked response in the guinea pig.

On the other hand, the second alternative suggested a careful study of the guinea pig's auditory area. Evidence stated above implied that the data of Kayrers and Legouix were probably not complete. As more investigators turn to the guinea pig as an experimental animal, the complete picture of the auditory area will become more important. Furthermore, Kayrers and Legouix failed to mention a number of facts that will be important in using evoked potentials in the search for an electronic prosthetic device. Among these facts are: anatomical variability of the auditory area; stability of the evoked potential over time; sharpness of the evoked potential threshold and the sound intensity needed to evoke a cortical potential. For these reasons, the cortex of the guinea pig was studied carefully in the present experiments. The cortex was studied for its own sake; it stands as a separate experiment. The results of the study of the guinea pig's auditory cortex will aid in interpretation of work pertaining to the electrical prosthetic device. The cortex work should also help in other areas of investigation.

In the present study of the auditory cortex, the effect of sound intensity upon the evoked potential was also studied. Evoked auditory potentials recorded from the cortex of humans (see Davis et al. 1966) increase in amplitude as the sound intensity is increased. A similar relationship occurs in the intensity function of the auditory nerve

in humans (Aran, 1970 Coats, 1970). Therefore, a general relationship seems to exist between the amplitude of an evoked potential and sound intensity.

If such a relationship is correct, the amplitude of an evoked potential may offer a means of equating the intensity of acoustical and electrical stimulation. Near threshold, for example, an electrical stimulus may evoke a cortical response whose amplitude is either similar to a weak or strong acoustical stimulus. This knowledge would be vital in behavioral studies in which transfer of training between acoustical and electrical stimuli are attempted.

Besides offering a method of comparing acoustical and electrical stimulation of the cochlea, the amplitude of the evoked cortical potential serves a second function. This second role is to aid in investigating the upper limit of the intensity range of the auditory system. Although large, the range of sound intensities to which the auditory system responds is finite. At the upper end of this range, human observers report pain and tactile sensations (for review see Licklider, 1951). However, these upper limits cannot be studied extensively in humans because intense sounds can permanently damage the cochlea. Therefore, in this study the cortical evoked potential as well as cochlear potential are used to study these upper limits.

The alternating cochlear potential is often used as a functional index of the inner ear. Just as psychophysical functions indicate that the auditory system responds to a finite range of intensities, the cochlear potential also has a finite range. At low and moderate

sound intensities, the intensity function is linear. A 20 db increase in the sound intensity will produce a 20 db increase in the amplitude of the cochlear potential. However, at higher sound intensities, this function departs from linearity. As Wever (1949) has shown, this departure is caused by distortion of the cochlear potential. Some of the acoustic energy imparted to the cochlea is shifted to both the odd and even harmonics of the stimulating frequency. The sum of the cochlear outputs at its fundamental frequency and its harmonics is a linear function with respect to sound. At even higher sound intensities, however, the cochlear potential reaches a maximum. Further increases in sound intensity, cause a reduction in the cochlear potential. This decrease is not caused by further distortion of the acoustic imput. Not only the fundamental, but also its harmonics decrease in amplitude. The actual cause of the decrease is unknown.

If the cochlear potential reflects the transducer function of the inner ear, the maximum and decrease seen in the cochlear potential should be reflected in the activity of neurons in the auditory pathway. The auditory evoked potential may be used as an index of this activity.

By recording gross evoked activity, Tunturi (1952) has found evidence that intensity of sound reaching the ipsilateral and contralateral ear are differentially coded in the auditory cortex of the dog. Previous to that study, Tunturi had noticed that the cortex of the dog was organized in isofrequency strips. Points along each strip had the same best frequency. As an electrode moved across adjacent strips, the best frequency of the response changed in a orderly fashion.

Tunturi felt that devoting a large strip of cortex to a single frequency was wasteful. Since nature is seldom so foolish, Tunturi looked for evidence that another quality of the auditory stimulus might be coded within a given strip of cortex. The logical candidate was stimulus intensity.

In order to investigate the effects of intensity upon the evoked potentials, Tunturi used a strychnine technique which be had developed earlier. He soaked a 1 mm^2 patch of filter paper in a 3% solution of strychnine sulfate. A toluidine blue or methylene blue dye was added to show the amount of strychnine diffusion. A single patch was placed on the cortex of the dog. After the application, strychnine spikes were recorded by a nearby electrode. The frequency of these spikes soon decreased to a low level. Once the cortex was quiet, certain acoustic stimuli could evoke strychnine spikes. A spike would be evoked if the acoustic stimulus activated a cortical area to which the strychnine had diffused.

A second position on the cortex cannot be studied until the strychnine at a previous spot lost its effectiveness. To reduce the time of deactivation, Tunturi washed the cortex with sodium pentothal.

Using these methods, Tunturi found that positions along an isofrequency strip had different thresholds for ipsilateral acoustic stimulation. A position near the suprasylvian sulcus had the lowest threshold. Cortical positions near the ectosylvian sulcus had higher thresholds. No difference in thresholds for contralateral stimulation was observed at various positions along the isofrequency strip.

In another study, Tunturi (1956) investigated the effect of stimulus intensity on the amplitude of the first positive wave of the evoked potential. In this study, he did not use strychnine. The amplitude of the first positive wave rose from a 100 uv at threshold to about 500 uv when the stimulus was increased 20 db. However, the amplitude of evoked potential was related to sound over only this restricted intensity range. In a review article, Tunture (1960) concluded that sound intensity was coded by increased amplitude for sound levels near threshold. Different fibers, however, appear to code the intensity of ipsilateral acoustic input throughout the intensity range.

In all of the above studies, the upper limits of the intensity range were not explored. In the present study, this upper range was studied.

These studies of the auditory cortex of the guinea pig set the stage for studies of electrical stimulation of the cochlea. By stimulating the cochlea electrically and recording the evoked potential, the approximate threshold for electrical stimulation could be obtained. One would know whether 1 uA or 1 mA were required to stimulate the nerve. The amount of voltage and/or current needed to stimulate the nerve at various frequencies would also be ascertained.

In order to quantify the stimulating current, an estimation of the impedance is needed. Geddes and Baker (1968) list three methods of measuring impedance in biological tissue. The simplest method requires passing a known constant current through the tissue. This

constant current can easily be provided by a high voltage source in series with a large resistor. With the constant current, the voltage drop across the animal can be measured. From this measurement the resistance can be computed by using Ohm's Law.

An impedance bridge can also be used to measure impedance. However, this method is more sensitive to changes in impedance than in the absolute level of the impedance.

A third method mentioned by Geddes and Baker requires the use of four electrodes. Von Bekesy (1951) used this method when measuring the impedance of the cochlea. In that method, a known current is passed through two electrodes. The voltage drop is recorded by two different electrodes located between the stimulating electrodes. According to Von Bekesy, an advantage of this method is that only a negligible current needs to flow through the recording electrode.

Von Bekesy found that the resistance from scala tympani to scala vestibuli in the guinea pig was 2.25 kilohms. The resistance from scala vestibuli to ground was 3.7 kilohms, while the resistance from scala tympani to ground was 8.5 kilohms. Von Bekesy said that he had found a 10% variation between animals in the resistance across the cochlear partition. A 20% variability in the resistance between the scalae and ground was found.

Von Bekesy also established that the cochlear partition behaved as a good electrical insulator. He had calculated that if the cochlear partition did not insulate at all, one would expect a 18 db/mm attenuation of an electrical signal (eg. cochlear potential).

Since only a 3 db / mm attenuation was observed, Von Bekesy concluded that the cochlear partition exhibited appreciable insulation. Other reports (Nakashima, Sullivan, Snow, and Suga, 1970; Kurokawa, 1965; Davis, 1957, and Wever, 1949) have also concluded that the basilar membrane as well as Reissner's membrane offer a large electrical resistance. On the other hand, Rauch, Kostlin and Schnieder, 1963; and Choo, and Tabowitz, 1965 have demonstrated that potassium can cross the membranes of the cochlear partition. So, although some direct current can be shunted through the cochlear partition, the basilar and Reissners membranes do serve as an electrical insulator.

Von Bekesy also determined the maximum current tolerable in the cochlea. He measured the cochlear potential after currents of various densities were passed through the inner ear. Von Bekesy found that current less than 3 ma did not depress the cochlear potential.

In the present study, the impedance of the electrical stimulating current will be estimated. Without such an estimate, the current values of the stimulus cannot be calculated. Since current will flow through both tissue and electrodes, the combined impedance will determine the amount of current for a given applied voltage. At high stimulating frequencies, the resistance of the tissue will contribute most of the total resistance. This impedance should be near the 2.25 kilohms observed by Von Bekesy. At lower stimulating frequencies, the electrodes should substantially contribute to the total resistance. Impedance should increase as the stimulus frequency is lowered.

The major goal of the electrical stimulation section of this project was simply the determination of thresholds for electrically evoked cortical potentials. The amplitude of the electrically evoked potential was also noted. This amplitude may serve as a very rough estimate of the loudness of an electrical stimulus that an unanesthetized animal might perceive. Finally, the evoked potential threshold for some cortical positions outside the auditory area was determined. By recording the threshold of an evoked potential outside the auditory area, the amount of current needed to stimulate non-auditory structures, such as the facial nerve, can be estimated. This level of current should serve as an upper limit of stimulus intensity.

In summary, three experiments related to the problem of developing an electrical prosthesis for patients suffering a sensorineural hearing loss are included in the dissertation. Two of the experiments are tangentally related to the main goal. Of these two tangental experiments, the map of the auditory cortex of the guinea pig is long overdue. As more investigators study the cortex of this animal, the map will serve as a necessary bit of basic information. The cortical intensity function is the second tangentally related project. Although a number of intensity functions in the auditory system have been reported, none of these studies used sound intensities which exceeded the intensity that produced the maximum cochlear potential. Since the cochlear potential goes through a maximum and then declines with further increases in sound intensity, it was felt that the rest of the auditory system may also show a similar reduction

in activity at these high sound intensities. The data demonstrating that such a reduction occurs in the amplitude of the evoked potential is an important contribution to the literature. Besides its own intrinsic merits, the cortical intensity function provides a means of comparing the intensity of the electrical and the acoustical stimulus. Finally, the third experiment was more directly related to the final goal. The threshold for electrically stimulating the cochlea was determined. Various positions for the stimulating electrodes were tried.

METHODS

Subjects

The subjects for these studies were 37 adult female guinea pigs obtained from the Oregon Regional Primate Center. Of these 37 guinea pigs,10 were employed to explore the auditory cortex with clicks, 10 were used to explore the cortex with tonal pulses, 9 were used to study the intensity functions of the cortex, and 8 were used for electrically stimulating the cochlea.

The guinea pigs weighed 400-750 gm. and were housed in the Animal Care facilities of the University of Oregon Medical School for several weeks prior to the experiment. A day or two before they were used, they were transferred to the Kresge Hearing Research Laboratory. The Preyer reflex was tested and found to be good in all animals immediately before they were used in the study.

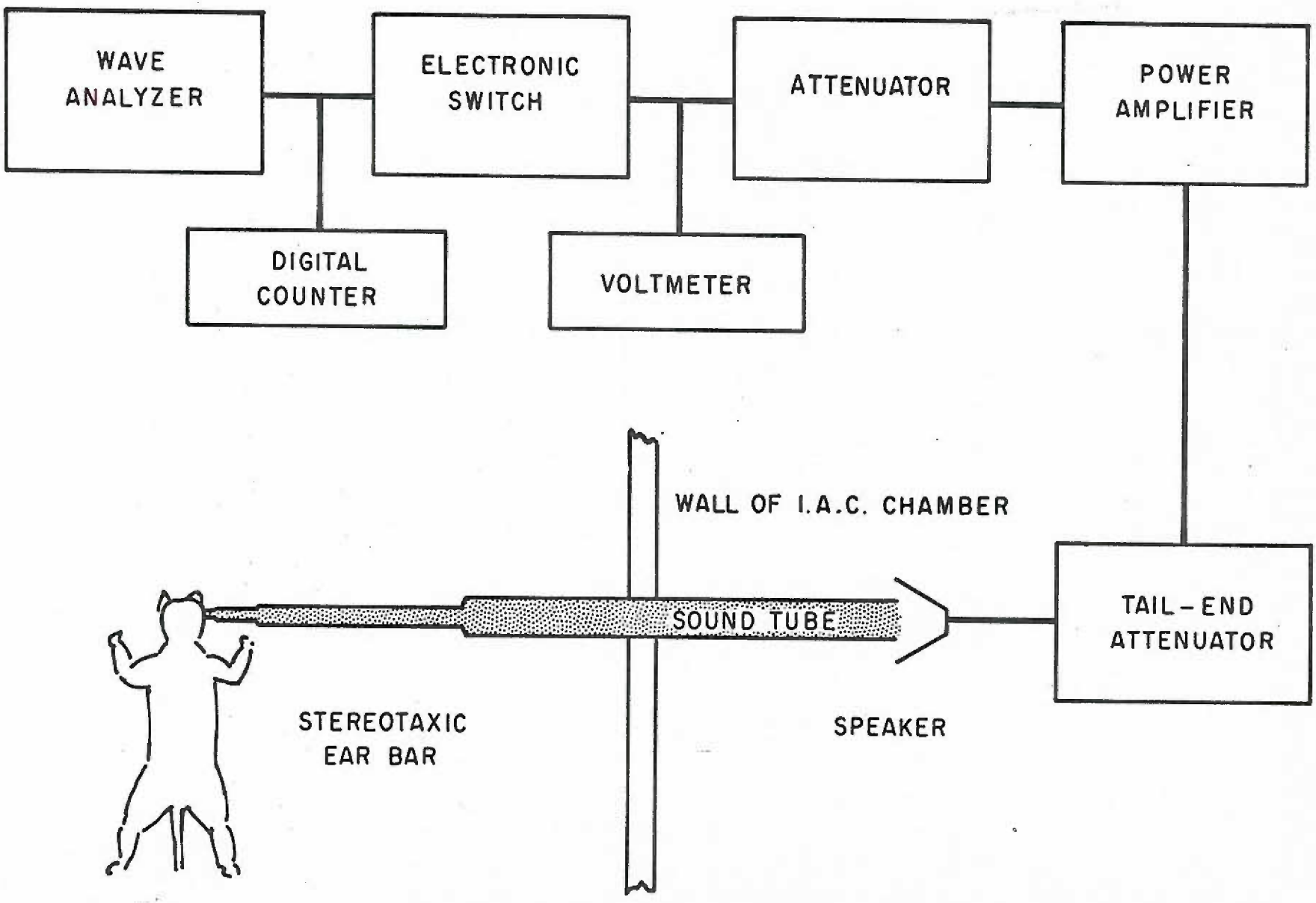
Apparatus

The experiment was conducted in a double-walled, sound-insulated Industrial Acoustics Company chamber. With the exception of the biological amplifier, all stimulating and recording equipment was located outside the chamber.

The sound producing system consisted of equipment which delivered an electronic signal of known dimensions to a Western Electric 555 speaker. This equipment is shown in Figure 1. The tracking oscillator of the General Radio Wave Analyzer (1900) provided the sinesoidal source for the sound. The exact frequency of the stimulus was measured with a Monsanto Digital Counter(103A) in order to maintain a $\pm$ 1Hz accuracy. A Grason-Stadler Electronic Switch (892E) and Interval Timer (147-I) were used to shape and time electronic pulses.

FIGURE 1

Schematic of the sound producing equipment. The tracking oscillator of the General Radio Wave Analyzer (1900) provided the sinesoidal waveform for the sound. The exact frequency of the stimulus was measured with a Monsanto Digital Counter (103A) in order to maintain a $\pm$ 1 Hz accuracy. A Grason-Stadler Electronic Switch (892E) and Internal Timer (147-I) were used to shape and time the electronic pulse. A Simpson voltmeter was used to monitor the intensity of the signal, and it was placed after the electronic switch. A General Radio Decade Attenuator (1450) was located before the Mc Intosch Power Amplifier (M-210-B). A specially built power or "tail-end" attenuator followed the amplifier. The sound transducer was a Western Electric 555 Speaker. A closed sound system connected this speaker with a hollow ear bar of the Stereotaxic unit. At the end of each day's study, the sound system was calibrated using a 1/4 inch Bruel and Kjaer microphone.


WAVE ANALYZER
ELECTRONIC SWITCH
ATTENUATOR
POWER AMPLIFIER
DIGITAL COUNTER
VOLTMETER
WALL OF I.A.C. CHAMBER
SOUND TUBE
TAIL-END ATTENUATOR
STEREOTAXIC EAR BAR
SPEAKER

For cochlear potential measurements, a continuous stimulus was utilized. On the other hand, a short pulse of approximately 50 msec was used for evoked potentials. A Simpson voltmeter was used to monitor the intensity of the signal, and was placed after the electronic switch. Since the voltmeter was placed before either of the two attenuators, it would monitor a constant 1 volt signal regardless of the sound intensities set by these attenuators.

Two attenuators were used to reduce the intensity of the stimulus. A General Radio Decade attenuator (1450) was located before the McIntosh Power Amplifier (M-210-B). A specially built power or "tail-end" attenuator followed the amplifier. This attenuator was needed to reduce the noise from the McIntosh amplifier. Without such an attenuator, pure tones of low intensity could not be presented to the animal. The output of the "tail-end" attenuator was led into the speaker.

The speaker was connected as a closed sound system to the hollow ear bar of a stereotaxic unit. In early experiments, a Labtronix Stereotaxic unit was employed. Later in the project, a Kopf instrument was used.

At the end of each day's work, the acoustic output of the sound producing equipment was measured. For this purpose,a 1/4 inch Bruel and Kjaer calibrated microphone was substituted for the animal at the end of the hollow ear bar. This position approximated the location of the tympanic membrane of the guinea pig. With the microphone and the General Radio Wave Analyzer, the intensity of the sound was measured. Throughout this paper, the sound intensity will be stated in decibels (db)

relative to one dyne/cm^2 or one microbar.

Biological potentials were initially amplified using a Keithley (103) differential amplifier. After this initial amplification, cochlear potentials were measured using the General Radio Wave Analyzer. Evoked cortical potentials, on the other hand, were displayed on a Tektronix 564B Storage Oscilloscope. At times, a Biomation 1000 Signal Analyzer was used to average the evoked potentials.

In order to stimulate the cochlea electrically, the same basic equipment was used as described above for acoustical stimulation. The wave analyzer, electronic switch, decade attenuator, Digital counter and voltmeter were used to produce and monitor the electronic pulse. In early experiments, the output of the decade attenuator was fed directly into the cochlea. In later experiments, an audio transformer was used to isolate the stimulus source. The use of a transformer between the decade attenuator and the cochlea helped prevent a ground loop. However, the use of this transformer did not appear to alter the effects of electrical stimulation.

Procedure for Mapping of Cortex

For the purpose of mapping the auditory cortex, the guinea pigs were deeply anesthetized with Dial Urethane (0.6 ml/Kgm[(1)]). Guinea pigs appear to be unusually vulnerable to the effects of anesthesia. Therefore, a tracheotomy was performed on all animals. Then when needed, artificial respiration was utilized. The rectal body temperature was constantly monitored and maintained at 38$\pm$ 1° C. Both pinnae were removed, to enable placing the animals in the stereotaxic

unit. The scalp and skull flap were removed to expose the entire left hemisphere. After the dura was reflected, warm mineral oil was allowed to flow across the cortex. In order to roughly define the limits of the auditory cortex, clicks were presented to the contralateral ear. A silver ball electrode (0.176 mm) was moved in 1 mm steps over the entire left hemisphere. Positions from which an evoked potential could be recorded were noticed.

After the gross limits of the auditory cortex were roughly defined, the auditory cortex within this area was studied in greater detail by using tonal pulses. Ten guinea pigs were used to establish the more refined and detailed map. It was now possible to reduce the extent of surgical involvement and expose only the temporal region of the left hemisphere. The remainder of surgical procedures were the same as described above. As in the rough map, the active electrode was moved in 1 mm steps over the entire temporal area. At each cortical position studied, the threshold for an evoked potential was obtained at each of the following frequencies: 100,200,300,500, 750, 1K, 1.5K, 2K, 3K, 5K, 7.5K, 10K, 15K, 20K, 25K, 30K, 35K, 40K.

Procedure for Cortical Intensity Function

A deeper level of anesthesia was used when studying the cortical intensity function than in the mapping experiments. After an initial dose of Dial Urethane (0.6 ml/K gm), all animals were placed on a mechanical respirator. Then, a supplimentary dose (1/4 to 1/2 the original dose) of the anesthetic was given. This supplimentary dose produced stage four anesthesia - that is, the guinea pig would not respire without mechanical assistance. This deep anesthesia reduced

the variability of the cortical electrical activity to very low levels. Of course, the animal did not move in response to any surgical procedure.

Both pinnae were removed and a post-auricular approach exposed both cochleae. One cochlea was prepared so that the alternating cochlear potential could be recorded, the other cochlea was destroyed with 10% formalin. The cochlea was destroyed to prevent contamination of the cortical record with activity evoked by sounds conducted through the skull. Since the cortex received both contralateral and ipsilateral innervation and since only about a 60 db attenuation is shown for sound conducted through the skull (Mast,1970 for the hamster), the contamination mentioned would occur if the ear had not been destroyed.

After an electrode had been placed with a micromanipulator on the round window of the non-damaged cochlea, it was secured to the bulla with dental acrylic. The guinea pig was placed in a stereotaxic instrument and the auditory cortex, contralateral to the non-damaged ear was exposed. After the dura was reflected, a silver ball electrode was lowered onto the pial surface of the cortex. This electrode was placed about in the center of the auditory area.

Intensity functions were not recorded simultaneously from the cochlea and the cortex. Rather, an intensity function was first obtained from the cochlea. Then, the intensity function of the cortical evoked potential was measured. Finally, the measurement of the cochlear intensity function was repeated to check on possible acoustic trauma. The entire process took from 10 to 20 minutes.

All of the intensity runs were made in an ascending order. Since the variability of the cochlear potential is negligible, a single run sufficiently defined the function. The large variability in the amplitude of the evoked potential (Tunturi, 1959; Howath, 1969) requires a number of runs for statistical reliability. In different animals, 10 or 20 ascending runs were made.

Procedure for Electrical Stimulation of Cochlea

The general surgical procedures were the same as described in the previous section, however, one cochlea did not have to be destroyed. Unlike sound, the electrical stimulus would not stimulate the opposite cochlea by bone or tissue conduction. The cochlea was exposed usually through both a post-auricular and a ventral approach. Two small holes,.08 to .13 mm in diameter, were drilled through the bone of the cochlea. These holes generally opened into the scala tympani, although a few opened into scala vestibuli. The holes were in either the basal turn or the apex. For bipolar stimulation, two platinum iridium wires (.08 mm) were inserted into the cochlea. These wires were secured to the bone of the cochlea with Ethicon(R) Adhesive. The wires were further secured to the bulla with dental acrylic. Cortical potentials were recorded in the usual manner.

Once the surgical preparations were completed, the following series of measurements were made. (1) A cochlear potential sensitivity function for the one microvolt level[2] was obtained for each intracochlear electrode. The frequencies used were 100, 300, 500, 1K, 3K, 5K, 10K, 15K and 25K Hz. (2) Then, the electrical impedance of

the cochlea-electrode complex was estimated. (3) The threshold for an acoustically evoked cortical potential was obtained. (4) The threshold of an electrically evoked cortical potential was then obtained. (5) Finally, the cochlear sensitivity functions were repeated. This final sensitivity function was made to check on any possible damage the electrical stimulus might have had upon the ear.

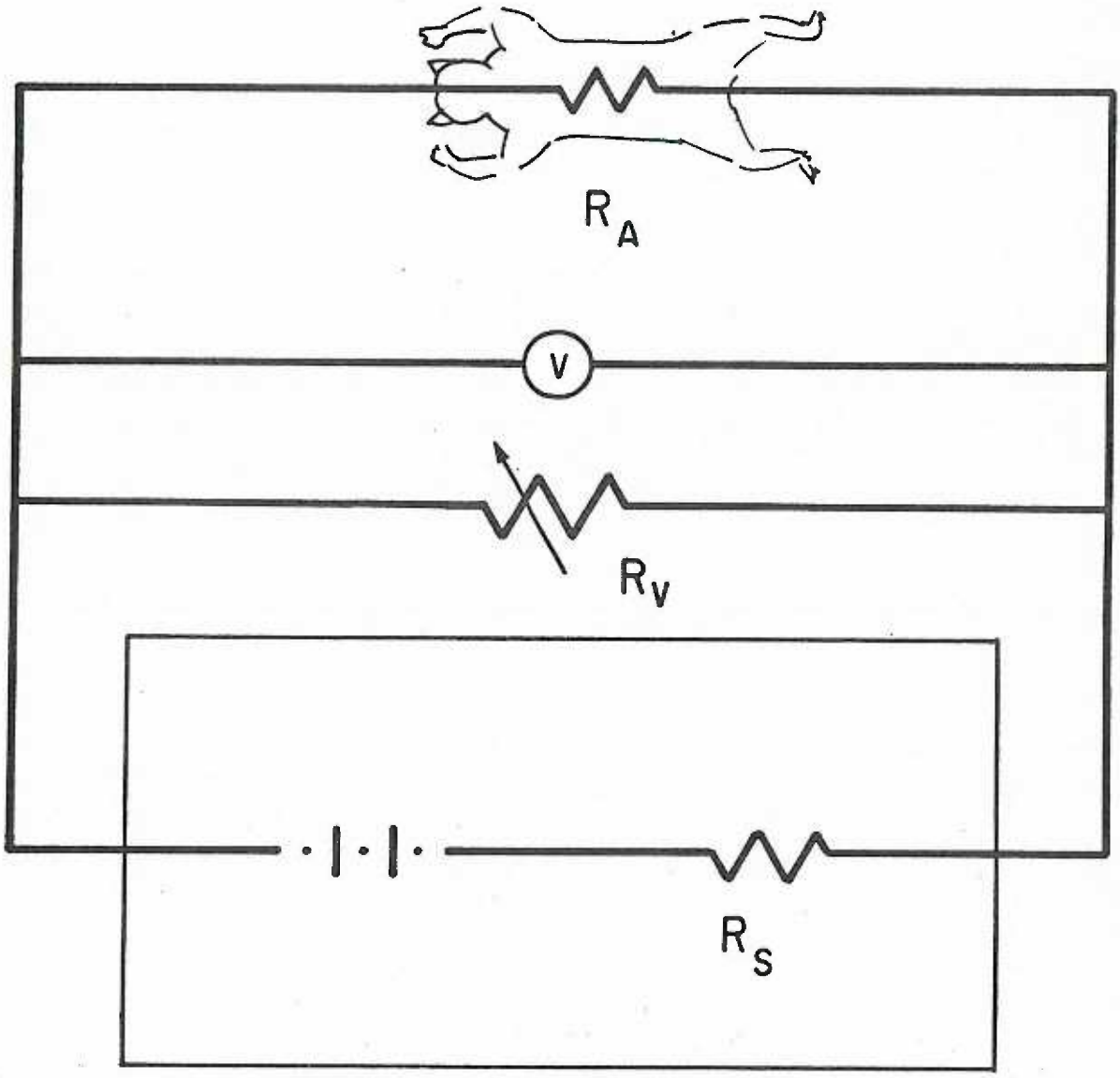
The measurement of evoked potential thresholds and cochlear sensitivity functions are standard laboratory procedures. However, the measurement of the impedance in the electrical stimulating circuit will be described in detail.

Figure 2 is a schematic of the apparatus that was used to estimate the electrical impedance. Essentially the equipment consisted of a constant current source, a voltage measuring device, and a variable resistor. A 100 meg ohm series resistor (Rs) essentially converted the circuit to a constant current source. The impedance of the animal and of the variable resistor made little difference in the total impedance of the circuit with this 100 meg ohm resistor in series. The variable resistor was in parallel with the animal. An oscilloscope was used to measure the voltage drop across the variable resistor-animal parallel circuit.

Conductance is the reciprocal of resistance. The total conductance of any parallel circuit of resistors equals the sum of the conductance of the parallel parts. In the present circuit, the total conductance equals the sum of the conductance of the guinea pig

FIGURE 2

Schematic for estimating the impedance in the circuit used to electrically stimulate the cochlea. The constant current source was provided by a 1 meg ohm resistor (Rs) in series with the tracking oscillator of the General Radio Wave Analyzer. The variable resistor (Rv) was simply a Heath Kit Resistance Substitution Box. A Tektronix Oscilloscope (V) was used to measure the voltage drop across the parallel resistances of the animal and the resistance substitution box.



CONSTANT CURRENT SOURCE

plus that of the variable resistor. From a theoretical standpoint, if the variable resistor is infinite, its conductance, $1/\infty$, is zero. Therefore, it does not contribute to the total conductance. On the other hand, the variable resistor could be adjusted so that its impedance would equal that of the guinea pig. Since these two equal conductances would add, the total conductance would be twice the conductance of the guinea pig alone. If the conductance is doubled the resistance (1/2c) is halved. Since the current is constant, Ohm's law predicts that the voltage across the animal is halved when the resitance is halved.

In practice, the variable resistor was set at 999K ohms. Then a current of known frequency but of unknown intensity was introduced. The current was raised until an easily readable record of the voltage drop could be obtained on the oscilloscope. Then the level of the variable resistor was reduced. At the setting that halved the recorded voltage, the level of the variable resistor equalled that of the animal. That setting was noted as the impedance of the animal at that particular stimulating frequency. This measure was repeated at each frequency used.

An isolation transformer did not separate the animal from the stimulus source in the initial experiments. Under these conditions a spurious ground loop was allowed in the stimulating circuit. Once the use of the transformer was initiated, this ground loop was eliminated. Differences resulting in the use of the transformer were of a small quantitative nature. The use of the isolation transformer did not effect the shape of the threshold curves for electrically evoked cortical potentials.

At the end of the experiment, the guinea pig was given a lethal dose of Beuthanesia(R). Before death occurred, the guinea pig was decapitated and the bulla with the intracochlear electrodes was removed. After removal, the bulla was opened widely. Some of the cochlear bone was fractured, in a manner similar to that done in a surface preparation. The cochlea was dissected until the tips of the stimulating electrodes could be observed. The positions of the electrodes were noted and often photographed. In some cases, the electrodes were dislodged as the cochlea was dissected. In these cases, only the cochlear partition could be examined for gross signs of disruption. Even when the electrodes had been dislodged, the approximate positions were known from the external anatomy of the guinea pig's cochlea.

RESULTS

Map of Auditory Cortex

Acoustically evoked potentials were recorded from a limited area of the guinea pig's cerebral cortex. In Figure 3B, the cortical evoked response to a click is shown. In these photographs, a positive deflection is in a downward direction. The first wave of these evoked responses was always surface positive. In the anterior portion of the auditory cortex, the initiation of this positive wave had a latency of 5 to 7 msec. The latency in the posterior portion of the auditory cortex was somewhat longer, 14-18 msec. The surface positive wave was followed by a surface negative wave. Only at high stimulus intensities, a second positive wave appeared. These click evoked responses were always restricted to the temporal area as indicated in Figure 4. For this reason, only the temporal area was studied in detail with tonal pulses.

Figure 3C is an example of cortical electrical activity to tonal pulses. The stimulus was a 25K Hz tonal pulse. The electrical signal to the speaker is recorded in the bottom trace. The middle trace is the evoked response to a -43 db tone. The top trace shows the cortical electrical activity when the intensity of the tone was reduced 10 db.

Figure 3D shows the evoked response to a 1K Hz tone. The top trace is the response to a -49 db tone. The middle trace is the response to a -39 db tone, while the bottom trace is the response to a -29 db tone. These figures are representative of all threshold

FIGURE 3

Record of the stimulus and evoked responses. Negative is up.(a) Averaged output of the calibrated microphone to a standard tonal pulse, showing that the sound pulse was free of on-set transients. (b) Superimposed cortical evoked response to clicks. (c) Cortical evoked response to a 25K Hz tonal pulse. Top line shows lack of a response to a -53 db tone. The middle trace shows a response when the intensity of the tone is increased to -43 db. The bottom line shows the signal. (d) Cortical response to a 1K Hz tonal pulse. The top line shows the absence of a response to a -49 db tone. An evoked response was obtained when the tone was -39 db, middle trace, and -29 db, bottom trace.

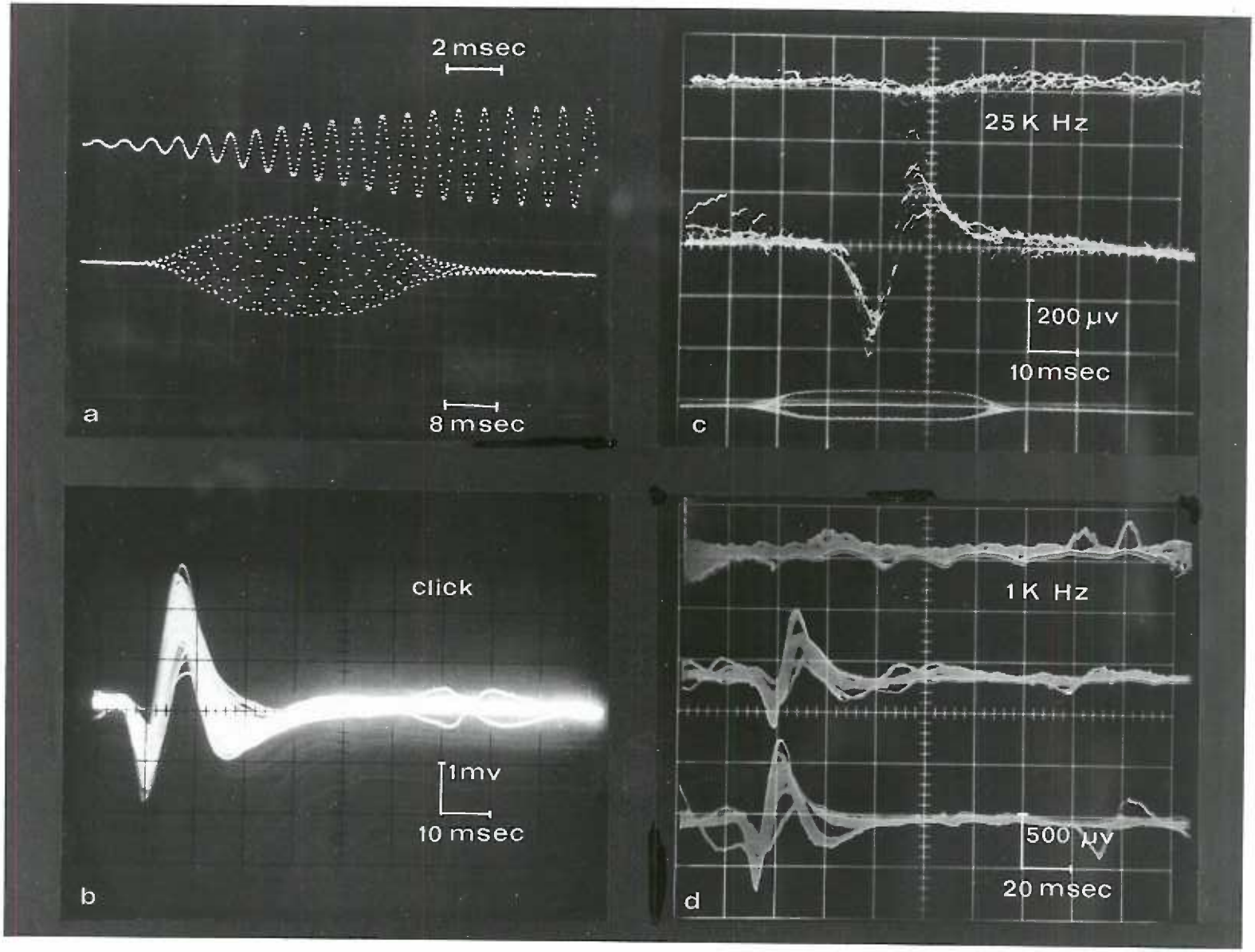
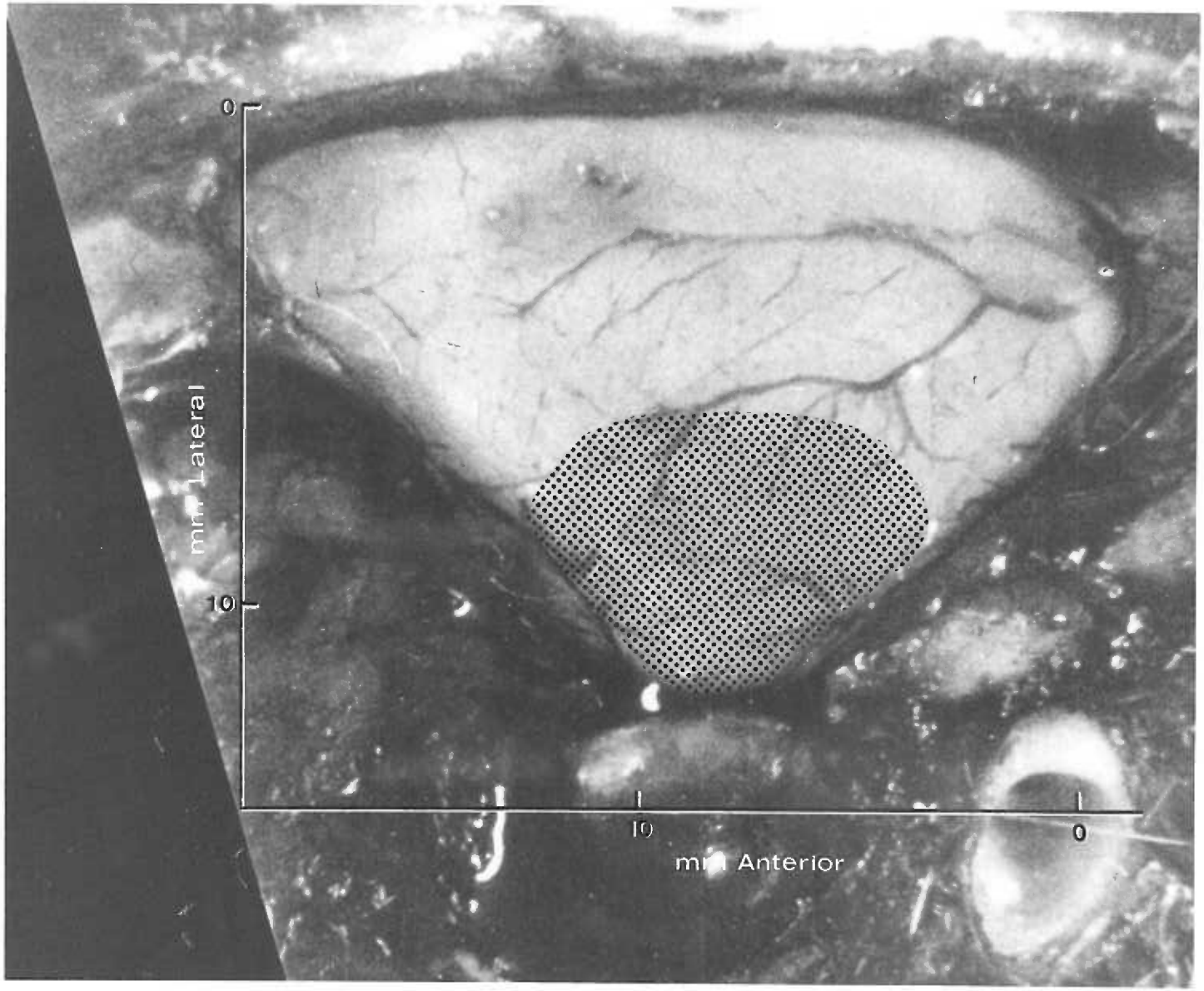

2 msec
a
8 msec
25 K Hz
200 µv
10 msec
c
click
1mv
10 msec
b
1 K Hz
500 µv
20 msec
d

FIGURE 4

The auditory cortex of the guinea pig. Cortical potentials evoked by clicks could be obtained from the shaded area. The external auditory meatus is marked by 0mm anterior. The midline is marked by 0mm lateral.


0
mm Lateral
10
10
0
mm Anterior

data. Stimulus frequency did not effect the sharpness of the threshold as seen in these data.

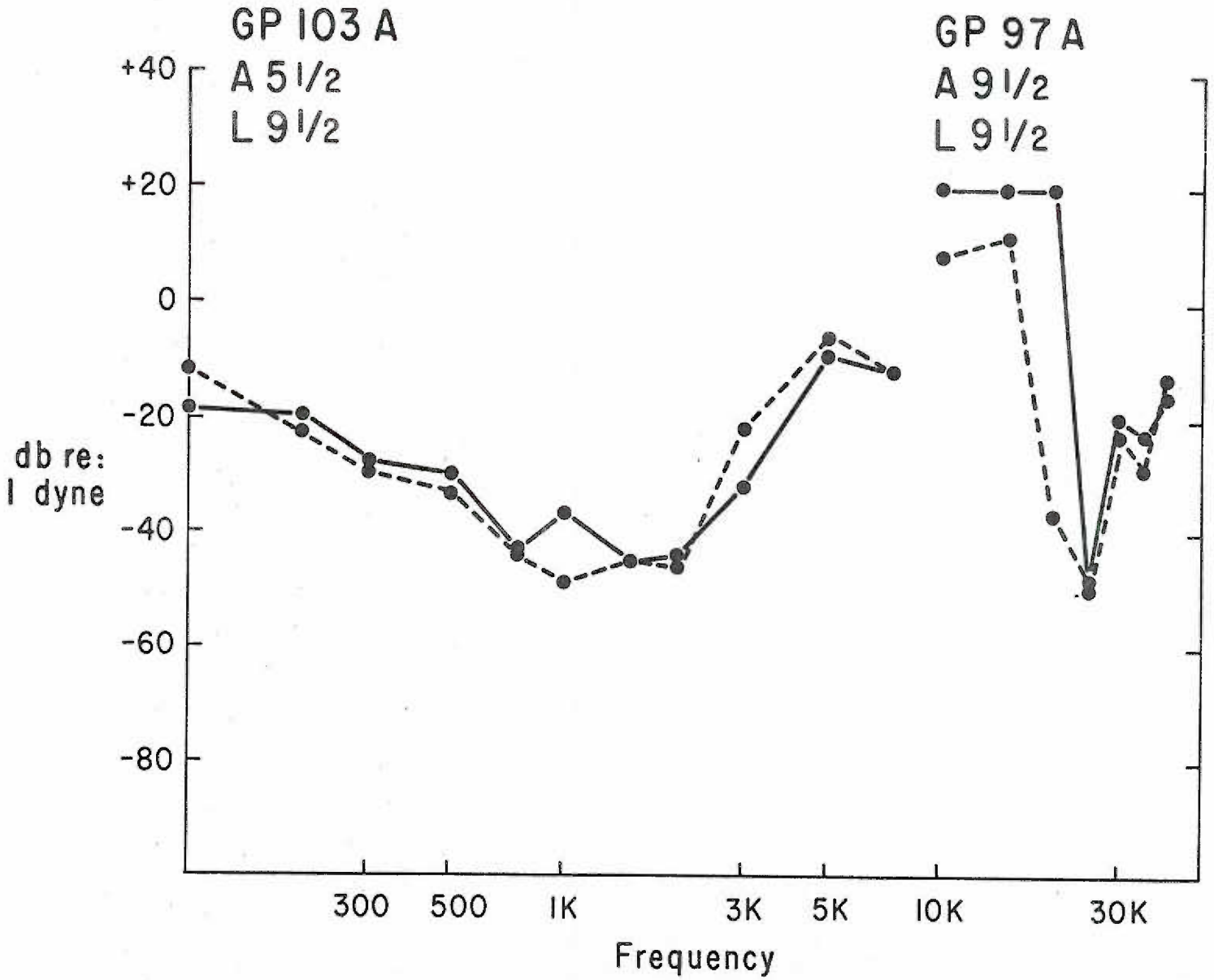
Figure 3 illustrates the sharp threshold of the acoustically evoked response. A 10 db reduction in the sound diminishes a 200-400 uv evoked potential to a level which cannot be detected even with averaging procedures. Within a 10 db limit, therefore, the threshold for an evoked potential is clear and unambiguous.

Not only were the thresholds of the evoked potential sharp and unambiguous, they were also extremely stable during the length of the recording session. Threshold curves obtained from two cortical positions are shown in Figure 5. While one cortical position had a best frequency of 1.5K Hz, the other cortical position's best frequency was 25K Hz. In order to check the stability of the evoked potentials, each of these threshold curves were obtained twice. The solid lines were obtained early in the mapping session. After the rest of the auditory cortex was investigated, the electrode was replaced at the indicated cortical position. Then, the threshold curve for that position was again obtained. At least 5 hours had elapsed between obtaining these two sets of data. Despite this lapse of time, the two curves are highly similar. Thus it is safe to conclude that the threshold values were very stable during the length of the recording session.

The limits of the auditory cortex when explored with tonal pulses were the same as the limits when explored with clicks (Fig 4). Although the auditory evoked potentials were confined to the temporal region of the cortex, the exact boundary of the auditory area varied

FIGURE 5

Typical threshold curves obtained from two positions on the cortex. Each threshold curve was obtained twice. The dashed curves were obtained 5 hours after the solid curves. For a given cortical position, therefore, the threshold for an evoked potential was very stable.


GP 103 A
A 5 1/2
L 9 1/2
GP 97 A
A 9 1/2
L 9 1/2
+40
+20
0
-20
-40
-60
-80
db re:
1 dyne
300
500
1K
3K
5K
10K
30K
Frequency

between animals. In Figure 6, the auditory area of each guinea pig is shown. The 10 mm marks serve as points of reference. They refer to cortical positions 10 mm anterior of the external meatus or 10 mm lateral of the midline. Each hash mark represents 1 mm. Both the shape and the total area of the auditory cortex varied. The variation of these areas, however, is no greater than that found in other cortical studies, such as those of the cat's auditory cortex. (Downman, Woolsey and Lende, 1960; Hind, 1953, Perl and Casby 1954).

The variation observed in the data probably reflect true anatomical differences. However, in order to ascribe these variations to anatomical differences, confidence must be obtained that experimental error has not significantly contributed to the observed variability. The single experimental error which could theoretically contribute most of the observed variability would be error in placement of the guinea pig in the stereotaxic apparatus.

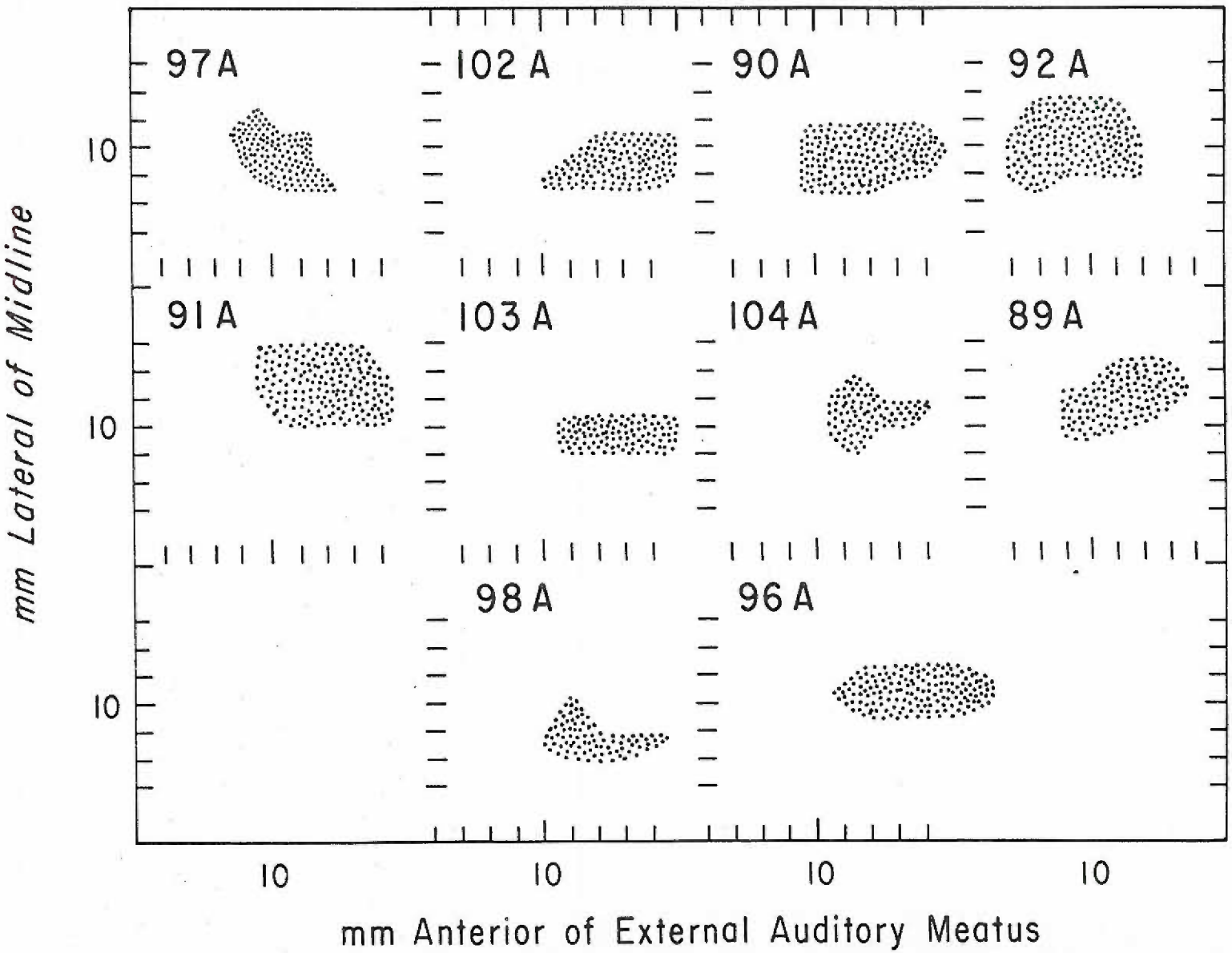
In the present study, errors due to incorrect stereotaxic placement could not be large. If the contralateral ear bar was not placed at the external bony meatus, sound would not have efficiently reached the tympanic membrane. Incorrect placement of the contralateral ear bar would, therefore, produce a very large reduction in the stimulus reaching the cochlea. However, in all animals, evoked potentials could be obtained at sound intensities of -40 to -60 db (Fig 5). Thresholds in this intensity range could not have been obtained if there was significant attenuation of the effective stimulus. Therefore, the contralateral ear bar must have been correctly positioned at the external bony meatus.

FIGURE 6

A representation of the variability in the cortical maps of the ten guinea pigs explored with tonal pulses. The 10 mm marks serve as points of reference. They refer to cortical positions 10 mm anterior of the external meatus and 10 mm lateral of the midline. Each hash mark represents 1 mm.

Inspection of the entire figure also reveals the variability in the location of the auditory cortex. For example, the responsive area of 92A is shown as located more anteriorly (to the left) than the area of 90A.

These differences in the size and location of the auditory cortex reflect true anatomical differences. Arguments favoring the acceptance of an anatomical basis for the observed variability are advanced in the body of the text.


97A
102A
90A
92A
91A
103A
104A
89A
98A
96A
10
10
10
10
10
10
10
mm Lateral of Midline
mm Anterior of External Auditory Meatus

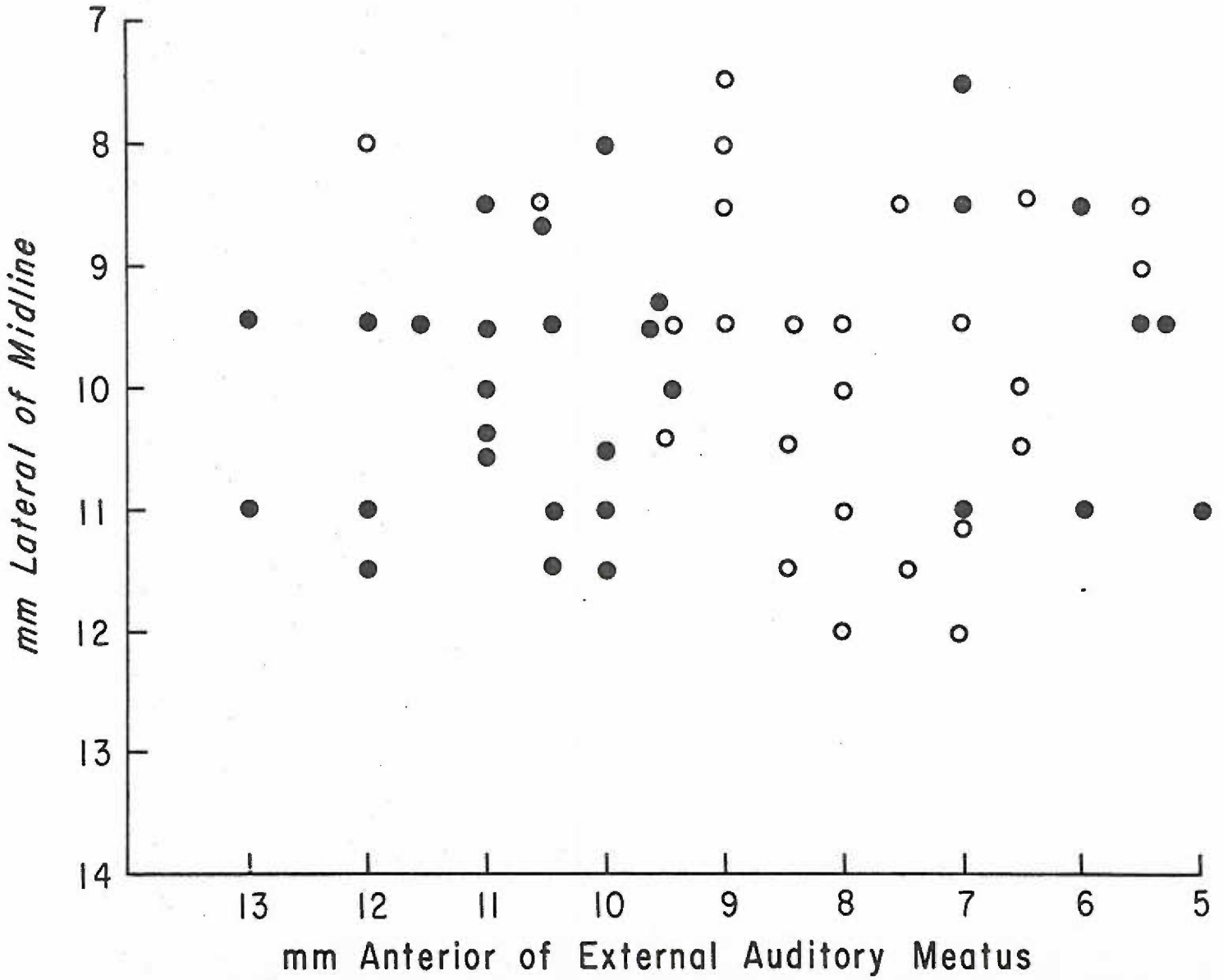
To insure correct placement of the ipsilateral ear bar, the alignment of the guinea pig's skull in the stereotaxic instrument was checked. In order to check this alignment, an electrode was used as a pointer and it was mechanically moved along the skull's mid-sagital suture. If the ipsilateral ear bar was properly placed, the mid-sagital suture would lie parallel to the anterior-posterior axis of the stereotaxic unit. Usually, no departure from the mid-sagital suture was noted as the pointer was moved along the anterior-posterior line. However, in a few cases, a departure of less than 1 mm was tolerated. Because of these precautions, confidence was obtained that incorrect placement of the guinea pig in the stereotaxic unit did not significantly contribute to the experimental error.

Although the location of the auditory cortex varied somewhat between animals, the organization within the auditory cortex was highly similar in all the animals. Figure 7, summarizes data obtained from the ten guinea pigs studied with tonal pulses. The closed circles indicate positions on the cortex which had best frequencies below 1.5K Hz. These positions were found in two regions. One region was more than 10 mm rostral to the bony meatus. The second region was less than 7 mm rostral to the bony meatus.

In Figure 7, the open circles indicate cortical positions whose best frequency was above 20K Hz. For the most part, these positions were found between 7 and 9.5 mm anterior to the bony meatus.

FIGURE 7

Pooled data from the ten guinea pigs investigated with tonal pulses. The closed circles are cortical positions whose best frequency was below 1.5K Hz. The open circles represent cortical positions whose best frequency was above 20K Hz.


7
8
9
10
11
12
13
14
mm Lateral of Midline
13
12
11
10
9
8
7
6
5
mm Anterior of External Auditory Meatus

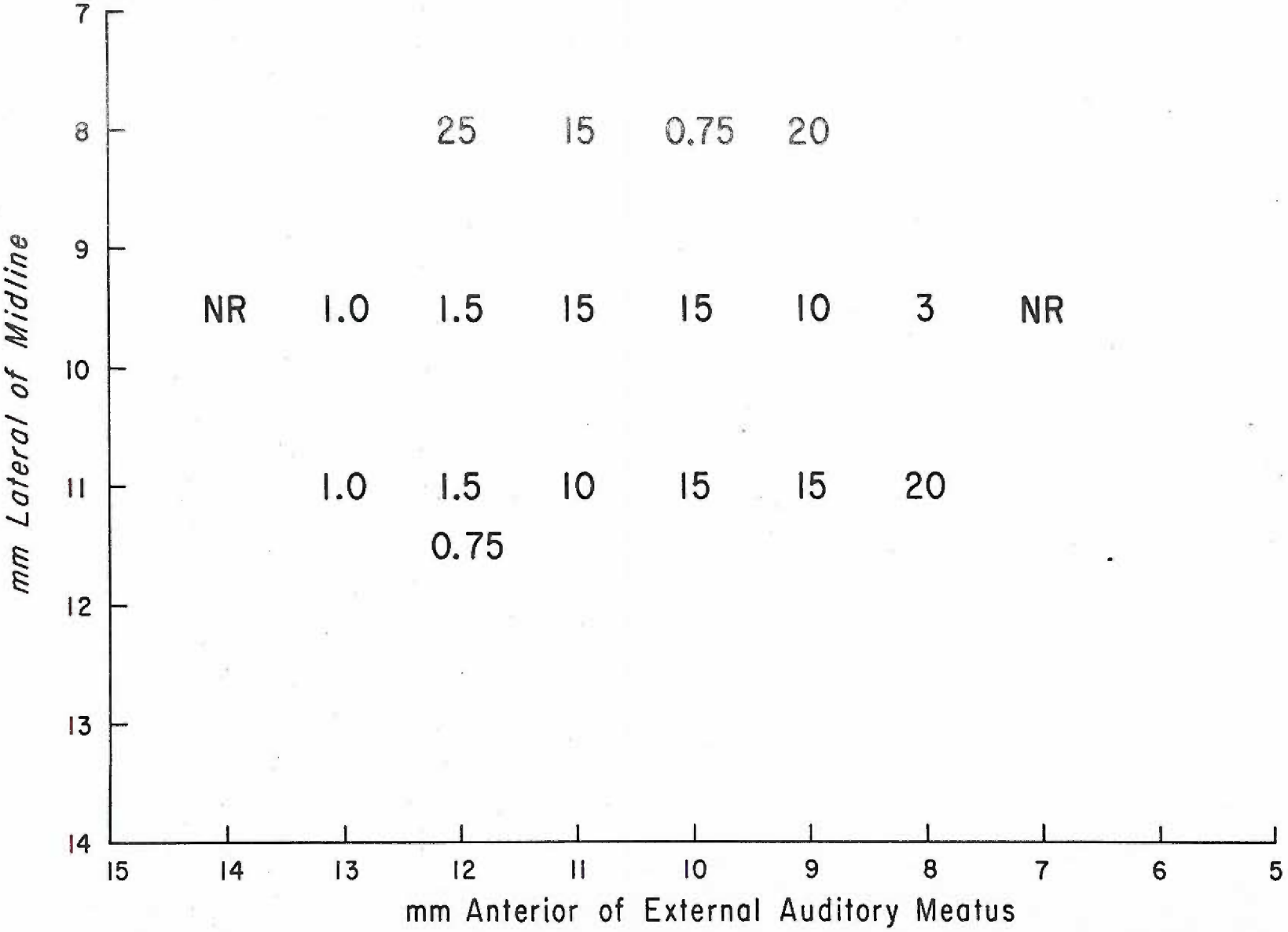
The pattern of cortical organization seen in the grouped data is also seen in the data from each individual guinea pig. Figure 8 shows the data from one representative animal. The numbers represent the best frequencies at the given cortical positions. As in the grouped data, anterior cortical positions were responsive to low frequency stimuli. However, the posterior area responsive to the low frequencies is represented by only one point (anterior 8 mm; lateral 9.5 mm). Although this posterior area was often limited to no more than one or two points, it was consistantly found in 9 out of 10 animals.

In this representative animal, the cortical position at 8 mm anterior and 11 mm lateral had a best frequency of 20K Hz. Such a high frequency point in the posterolateral position of the auditory cortex was found in all 10 guinea pigs. Moreover, an orderly progression of best frequencies can be seen along the lateral border of the auditory cortex. This type of progression was also seen in all 10 guinea pigs. Although the orderly progression of best frequencies along the lateral border and the high best frequency at the most posterolateral point of the auditory cortex are clearly seen in each individual record, these facts are slightly obscured in the pooled data of Figure 7.

One must always be cautious when inferring the existence of auditory areas or tonotopic regions from a given set of observations. The present data seem to clearly indicate two areas that are responsive to the low frequencies. Therefore, the existence of two tonotopic areas is very probable. The portions of these tonotopic areas

FIGURE 8

The auditory cortex of one representative animal. The numbers represent the best frequency of the cortical position in kilohertz. The posterior region responsive to low frequency stimuli is represented by only one point (A8 L9 1/2). Although this representation by a single position was often the case, a low frequency point was consistently observed in 9 out of 10 animals. In this guinea pig, the most posterolateral position (A11 L8) was responsive to high frequency tonal pulses. Such a high frequency point was observed in all 10 animals.


7
8
9
10
11
12
13
14
mm Lateral of Midline
25 15 0.75 20
NR 1.0 1.5 15 15 10 3 NR
1.0 1.5 10 15 15 20
0.75
15 14 13 12 11 10 9 8 7 6 5
mm Anterior of External Auditory Meatus

that are responsive to the high frequencies may border each other in the center of the auditory cortex (Fig. 7 - anerior 8 mm; lateral 10 mm).

Although the frequency data supports the existence of two tonotopic regions, similar to those proposed by Kayrers and Legouix, a different organization could be present. For example, a third tonotopic area could lie along the posterior border of the auditory cortex. Along this border, latency of the evoked potential for click stimulation is long. So, although an auditory area along the posterior border may not be evident from the pooled frequency data, an analysis of the latency data may confirm its existence. Similarly, the progression of frequencies along the lateral border may suggest a third auditory region.

In summary, acoustically evoked potentials can be recorded from the temporal region of the guinea pig's cortex. The thresholds for the evoked potentials were unambiguous and stable during the recording session. Some anatomical variation in the location of the auditory cortex was found. The data indicate the probable existence of two tonotopically organized areas. Some evidence indicates the possible existence of a third tonotopic area.

Cortex Intensity Function

The evoked potentials recorded from the auditory cortex were not only influenced by changes in stimulus frequency but also by changes in sound intensities. In fact, intensity functions obtained from the auditory cortex were very similar to the intensity functions of the cochlear potential. These functions from a representative animal are shown in Figure 9. Similar figures from other animals appear in Appendix 3. The solid line is a cochlear potential

obtained immediately before the cortical measure. The dashed line, on the other hand, is a cochlear function obtained immediately after the cortical measure.

On log-log coordinates,[3] these cochlear intensity functions are linear between -43 and -13 db. Above -13 db, the cochlear potential departs from linearity. With further increases in sound level, the cochlear potential plateaus. Above +18 db, an increase in sound intensity reduces the amplitude of the cochlear potential.

The amplitude of the cortical evoked potential behaved in a similar manner. In Figure 9, the cortical evoked potential is plotted on semi-log coordinates. The amplitude of the evoked potential increases as the sound intensity is raised from -23 to +18 db. When the sound intensity was further increased to +28 db, the amplitude of the evoked potential was reduced.

The pattern of responses obtained from the representative animal shown in Figure 9 was also obtained from the other six animals. As expected, all the cochlear potential intensity functions portrayed the typical "bend-over" or reduction in amplitude at high intensities of sound. Moreover, most ascending runs for the intensity function of the evoked cortical potential also showed a reduction or "bend-over" at high sound intensities. The exact percentage of runs for each animal which showed such a reduction in evoked potential amplitude is listed in the lower part of Tables 1 and 2. While Table 1 lists the results obtained when a 10K Hz acoustic

stimulus was used, Table 2 summarizes data obtained with 1K Hz stimulation.

In this study, 13 intensity functions were obtained. Generally, a 1K Hz and a 10K Hz intensity function were obtained from each animal. A sign test was used to determine whether or not the reduction in the amplitude of the evoked potentials observed at high intensities were significant. For the purpose of this non-parametric statistic, the amplitudes of the evoked potential at two stimulus intensities were compared. One of each pair of cortical potentials was evoked by the sound intensity needed to produce the maximum cochlear potential. The second cortical potential of each pair was evoked by a more intense stimulus. For 10K Hz stimulation, a 10 db difference separated the sound intensities that evoked the two cortical potentials. At 1K Hz, a 20 db difference was needed.

For 11 of the 13 pairs of evoked potentials examined, the higher sound intensity produced the smaller amplitude evoked potential. A sign test indicated that this datum was significant ($p<.01$). Combining the data from 1K Hz and 10K Hz stimulation did not seriously infringe on the independence of observation since 1K Hz and 10K Hz are for the most part coded in different auditory nerve fibers and on different portions of the basilar membrane.

In Tables 1 and 2, the sound intensity needed for a maximum cochlear potential and a maximum evoked cortical potential are also listed. For 10K Hz, the maximum evoked potential usually occurred at a slightly lower intensity than the maximum cochlear potential. The mean difference was 8 db, and the largest difference observed was 19 db. For 1K Hz, the maximum evoked potential occurred at a sound level that was 2.2 db more intense than that needed for the maximum cochlear potential. A 18 db range was found. Therefore, the cochlear potential and the evoked cortical potential reached a maximum at about the same sound intensity.

Unfortunately, the stimuli needed to measure these cortical potentials appeared to damage the ear. In all cases, some depression of the cochlear potential was observed. However, the reduction seen in the amplitude of the evoked potential was probably not due to the injury to the ear. The amplitude reduction was seen in the first few trials, when the injury to the ear was slight as well as in the later trials, when the injury had progressed.

In summary, the intensity function of the evoked cortical potential is similar to that of the cochlear potential. At low and moderate sound intensities, the amplitude of both potentials are directly related to the stimulus level. An

FIGURE 9

Intensity functions of the cochlear potential and the gross evoked potential recorded from a representative animal. One of the intensity functions for the cochlear potential was recorded before the evoked potentials were recorded. To check for possible acoustic trauma, a second intensity function was obtained after the evoked potentials were recorded. In this animal, little acoustic trauma was observed.

The mean and standard deviation of the evoked potential are plotted. In this animal, twenty ascending intensity runs were used to obtain these data.

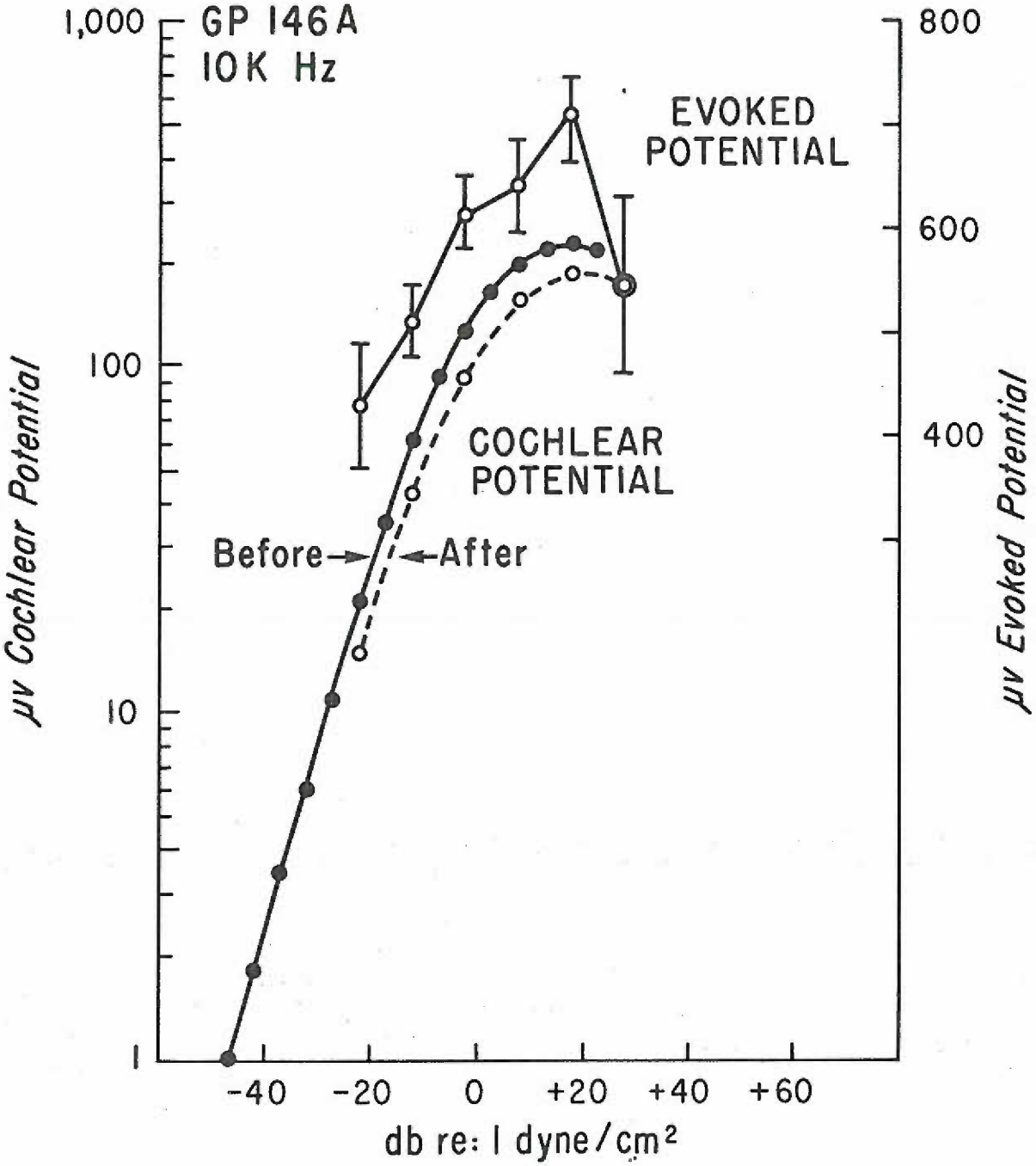

GP 146A
10K Hz
EVOKED
POTENTIAL
COCHLEAR
POTENTIAL
Before
After
1,000
100
10
1
800
600
400
μv Cochlear Potential
μv Evoked Potential
-40
-20
0
+20
+40
+60
db re: 1 dyne/cm²

TABLE 1

Table 1 - lists data for the 10K Hz intensity functions. The animals are identified by number. The sound intensity needed for a maximum cochlear potential (CP) and a maximum evoked potential (EP) are indicated.

In the lower part of the table, results of individual ascending runs used to obtain the intensity functions of the gross evoked potential are summarized. The percentage of runs that showed a "bend-over" or reduction in amplitude at high stimulus intensities are listed. Since the total number of runs were not equal for all animals, this datum is also shown.

Animal Number	127	131	140	142	145	146	147
db for CP* Max	+18	+18	+24	+32	+30	+18	+26
db for EP** Max	+18	+ 3	+ 9	+13	+20	+18	+31
% Runs Bent Over	80	100	89	90	90	85	75
Total Number Runs	20	20	10	10	19	19	20

*Cochlear Potential
**Evoked Potential

TABLE 2

Table 2 - lists data for the 1K Hz intensity functions. The animals are identified by number. The sound intensity needed for a maximum cochlear potential (CP) and a maximum evoked potential (EP) are indicated.

In the lower part of the table, results of individual ascending runs used to obtain the intensity functions of the gross evoked potential are summarized. The percentage of runs that showed a "bend-over" or reduction in amplitude at high stimulus intensities are listed. Since the total number of runs were not equal for all animals this datum is also shown.

Animal Number	127	131	142	145	146	147
db for CP* Max	+37	+51	+41	+48	+43	+44
db for EP** Max	+47	+52	+46	+35	+44	+53
% Runs Bent Over	95	80	50	90	75	100
Total Number Runs	19	9	10	20	20	20

*Cochlear Potential
**Evoked Potential

increase in the intensity of the sound will produce an increase in the amplitudes of the cochlear potential and of the cortical evoked potential. However, this direct relationship holds only up to a certain sound intensity. Further increases in the sound above that point reduced the amplitude of both the cochlear potential and the cortical evoked potential.

Electrical Stimulation of the Cochlea

In most attempts to electrically stimulate the cochlea, both electrodes were placed in the scala tympani of the basal turn. In one individual, the electrodes were placed across the cochlear partition of the basal turn. While one electrode was in the scala tympani, the other electrode was in the scala vestibuli. Finally, the electrode placements in two guinea pigs spanned the length of the cochlea. One electrode was in the scala tympani of the basal turn; the other electrode was in the apex. While an apical electrode can not be easily placed in humans, the other electrode positions have already been clinically employed.

As in the case of sound evoked potentials, the threshold for an electrically evoked cortical potential was sharp and unambiguous. Figure 10a illustrates the crispness of the evoked potential threshold. Sixteen superimposed responses to a 1K Hz electrical stimulus are shown in this figure. One of the stimulating electrodes was located in the scala tympani of the basal

turn, while the other electrode was in the apex. The top trace shows a 1 mv response to an electrical stimulus that was -26 db re 1 volt. When the stimulus was reduced to -29 db, no cortical response was elicited (lower trace).

Threshold curves were successfully obtained from five guinea pigs with both electrodes implanted in the scala tympani of the basal turn. Figure 10b and 10c are photographs of typical electrode placements. The entire cochlea can be seein in Figure 10b.

The base and the apex have been fractured to allow perfusion of the cochlea and inspection of the electrode sites. One electrode can be clearly seen entering the scala tympani of the basal turn. The other electrode also enters at about the same location, although it is difficult to see in the photograph. Neither electrode infringed upon the basilar membrane.

In Figure 10c, a more restricted view of the cochlea is shown. Both the round window and the oval window can be identified. Again, the two stimulating electrodes are in the scala tympani of the basal turn. While one electrode is clearly suspended in the perilymphatic space, the other may infringe on the basilar membrane complex.

With electrodes in the scala tympani of the basal turn, the threshold curves shown in Figure 11 were obtained. At 10K Hz, all the thresholds for electrically evoked potentials were below 40 uA.

FIGURE 10

(a) illustrates the sharpness of an electrically evoked potential. The stimulus frequency was 1K Hz. The top trace shows an evoked cortical potential to an electrical stimulus that was -26 db re 1 volt. When the stimulus was reduced 3 db, the evoked potential could not be observed. The peak to peak amplitude of the top trace was about 1 mv. (b) photograph of the stimulating electrodes in the scala tympani of the basal turn. One electrode can clearly be seen in the perilymphatic space. The other electrode is difficult to identify in this photograph. (c) photograph of the stimulating electrodes in the scala tympani of the basal turn in a different animal. While one of the electrodes is clearly in the perilymphatic space, the other electrode may infringe upon the basilar membrane complex. (d) photograph of a stimulating electrode in the apex.

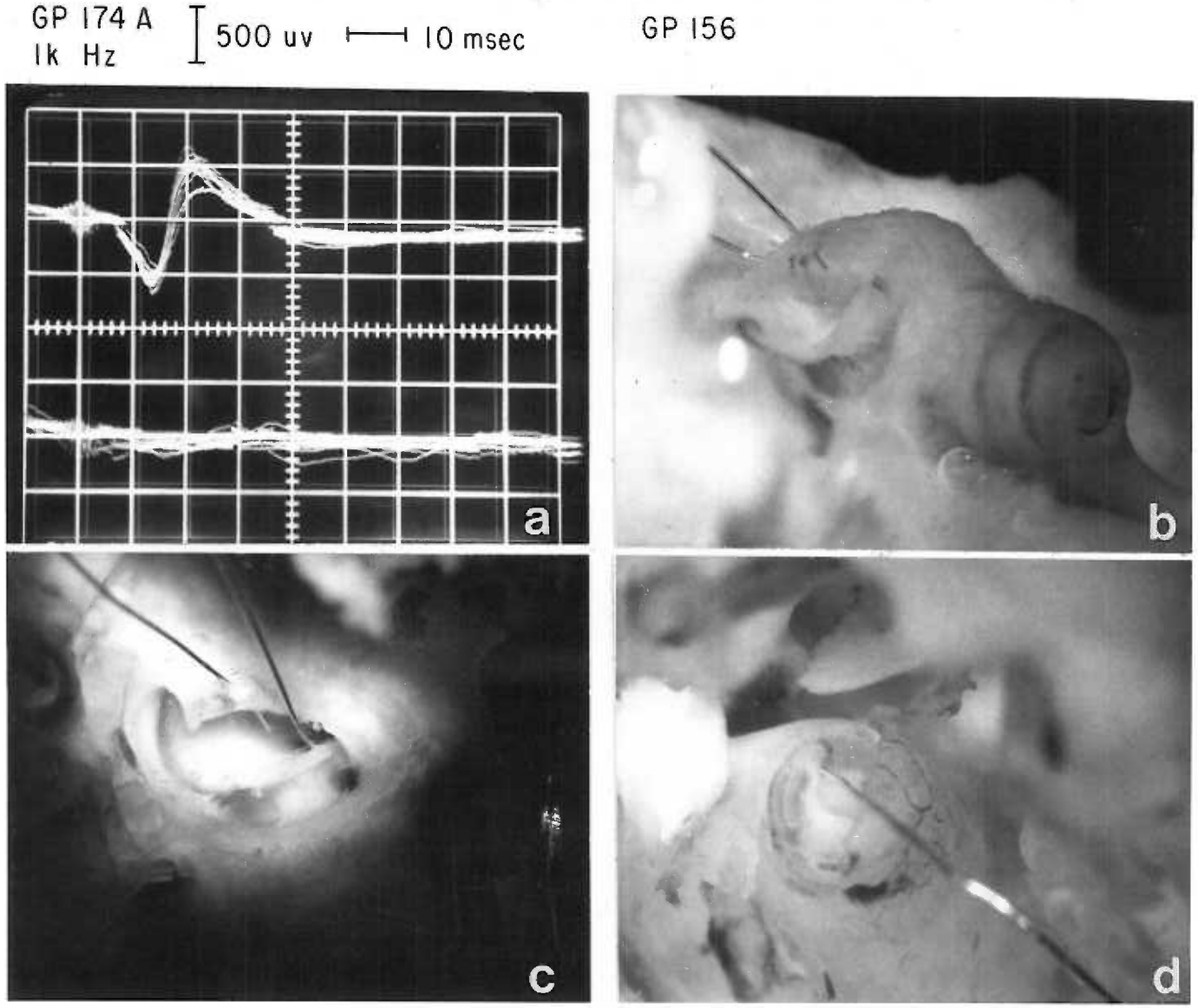
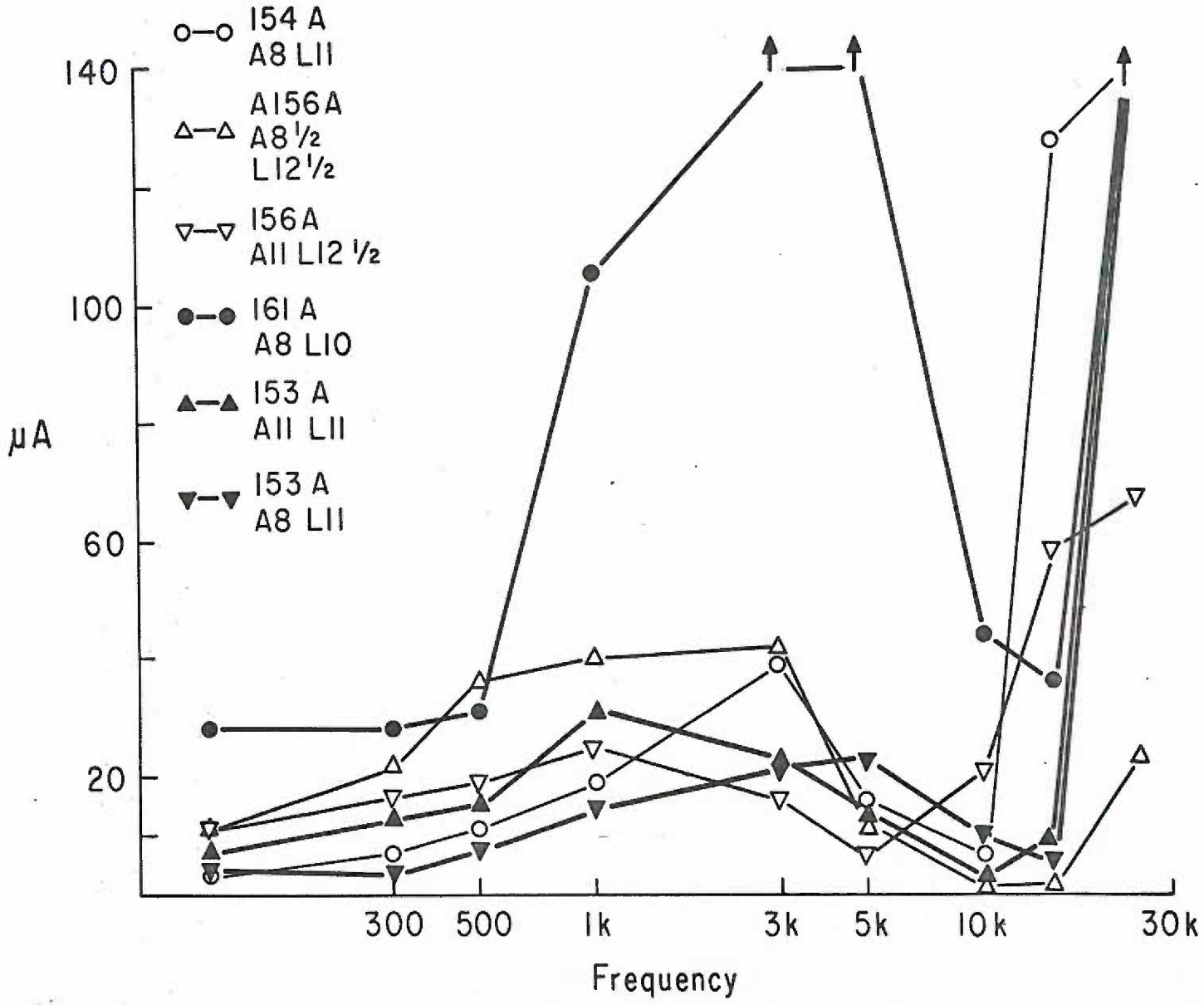

GP 174 A
1k Hz
500 uv
10 msec
GP 156
a
b
c
d

FIGURE 11

Threshold curves for electrical stimulation of the cochlea. Both stimulating electrodes were located in the scala tympani of the basal turn. At the left, the animals as well as the position on the cortex from which the recording was made are indicated.


154 A
A8 LII
A156A
A8 1/2
L12 1/2
156A
AII L12 1/2
161 A
A8 LIO
153 A
AII LII
153 A
A8 LII
140
100
60
20
μA
300
500
1k
3k
5k
10k
30k
Frequency

This low threshold was unexpected.

In all but one animal, the threshold for an electrically evoked potential was below 45 uA at all frequencies lower than 10K Hz. The threshold curves are relatively flat, although a slight increase in the threshold is seen at the mid-frequencies (1K Hz to 3K Hz). In one animal, this increase of the threshold at the mid-frequencies is greatly exaggerated. Even in this individual, however, a very low threshold for an electrically evoked potential is seen at both the low and the high frequencies.

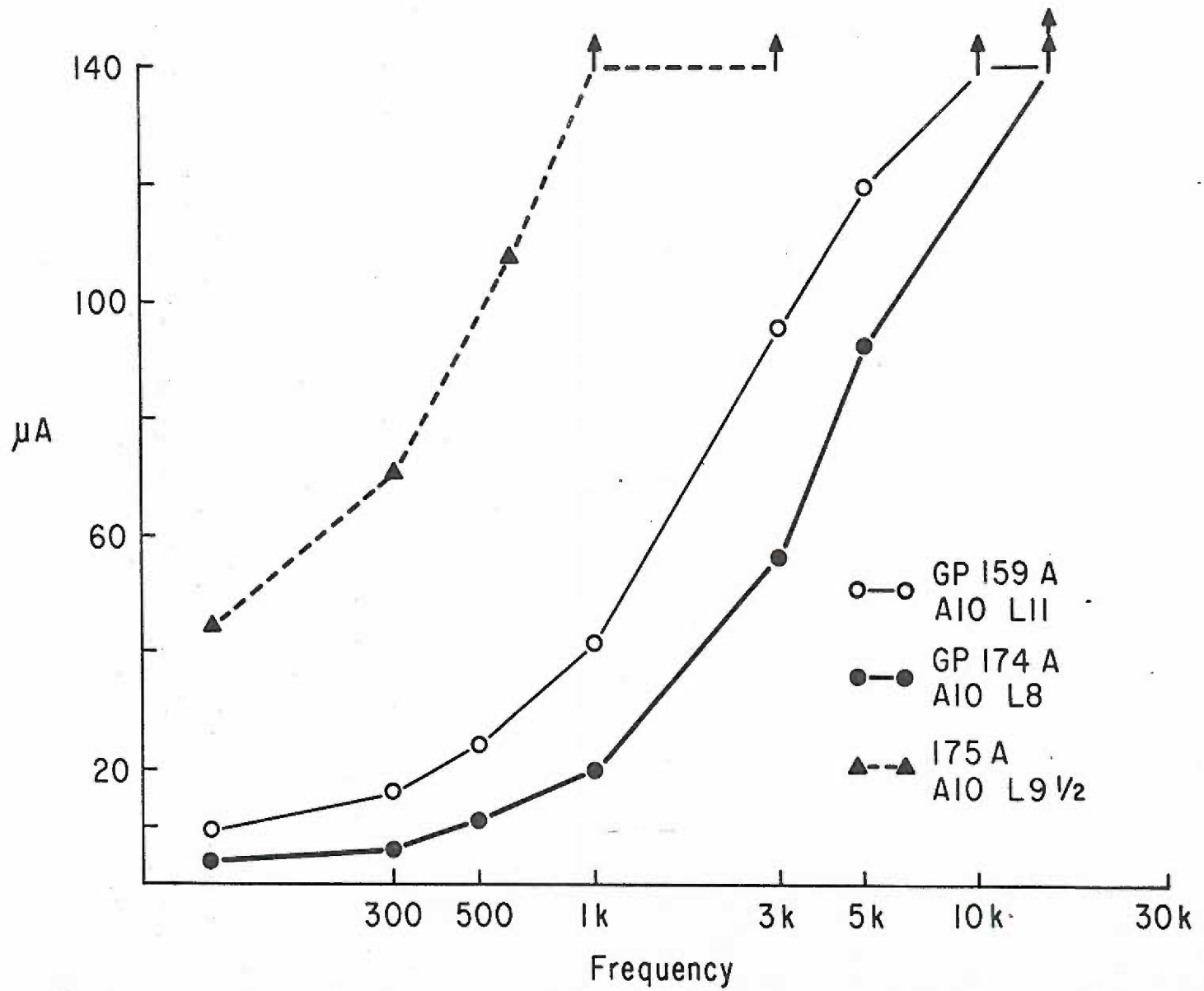
In two guinea pigs, the two stimulating electrodes spanned the length of the cochlea;while one electrode was in the scala tympani of the basal turn, the other electrode was located in the apex. Figure 10d is a photograph of an apical electrode placement. Some of the bone from the apex of the cochlea had been removed to allow inspection of the electrode site. The basilar membrane of the fourth turn can be seen directly below the tip of the electrode. Therefore, the electrode is either at the helicotrema or in scala vestibuli of the fourth turn.

The apical electrode was difficult to implant. In comparison with the electrodes placed in the scala tympani of the basal turn, an apical electrode was severely cramped. Verification of the electrode placement in the apex was also more difficult than in the base. Often disection of the bone at the apex, dislodged the electrode.

The solid curves of Figure 12 show the thresholds for electrically stimulation between the apex and base. These similarly appearing threshold curves were obtained from separate animals. At low stimulus frequencies, the threshold for an electrically evoked

FIGURE 12

Threshold curves for the electrical stimulations of the cochlea. The two solid lines were obtained with one stimulating electrode in the apex. The other stimulating electrode was in the scala tympani of the basal turn. The dashed function was obtained with stimulating electrodes that spanned the cochlear partition. One electrode was in scala tympani of the basal turn while the other electrode was in scala vestibuli of the basal turn. The animal number, and the cortical position from which the recordings were made are indicated.


140
100
60
20
μA
300
500
1k
3k
5k
10k
30k
Frequency
GP 159 A
A10 L11
GP 174 A
A10 L8
175 A
A10 L9 1/2

potential was below 10 uA. In this respect, the thresholds were similar to those obtained when both electrodes were in the scala tympani of the basal turn. However, the threshold for an electrically evoked response rises sharply for stimulus frequencies above 1K Hz. At 10K Hz, the threshold is greater than 140 uA. This 140 uA level is very different from the 40 uA threshold obtained at 10K Hz when both stimulating electrodes were in the scala tympani of the basal turn.

In a separate guinea pig, the stimulating electrodes were placed across the cochlear partition. One electrode was in the scala vestibuli of the basal turn, while the other was in the scala tympani. With these electrodes, the dashed curve of Figure 12 was obtained. Although somewhat elevated, it has the same shape as the threshold curves obtained by stimulating between the base and the apex.

Theoretically, an electrical current passed through the cochlea can evoke a cortical potential in three ways. The current could (1) depolarize the auditory neurons and thus trigger the nervous activity directly. (2) The current may depolarize the hair cells and stimulate the nerve indirectly. On the other hand, (3) if the current could produce movement in the cochlear fluids, the auditory system would respond to the current-induced movement as if it were sound. John Epley (private communications) has suggested that current-induced fluid movement might have been involved in one of Simmon's studies (1964).

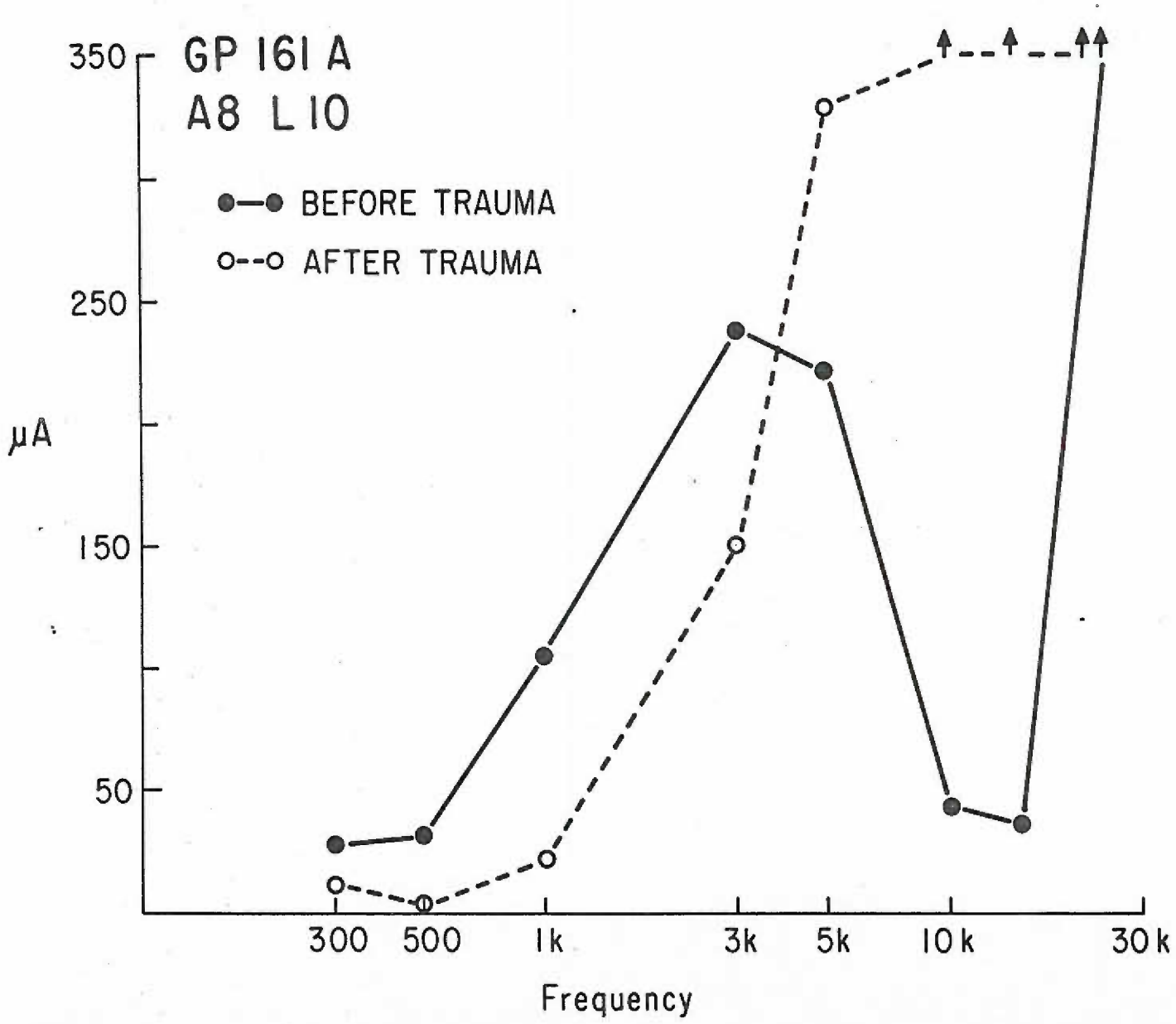
A damaged cochlea that could no longer respond to sound would not be able to respond to current-induced fluid movement. Therefore after the thresholds for an electrically evoked potential were obtained from a guinea pig with an undamaged cochlea, a +74 db, 1K Hz tone was presented for 30 minutes. After the presentation of this very intense tone, sound could no longer evoke a cortical potential. Before the acoustic trauma, a -60 db, 15K Hz tone could evoke a response from the cortex.

Data from this animal are presented in Figure 13. The solid curve was obtained before the acoustic trauma. At 10K and 15K Hz, the thresholds for an electrically evoked potential were below 45 uA. In Figure 13, the dashed curve was obtained after acoustic trauma. At 10K and 15K Hz, the thresholds for an electrically evoked potential was greater than 350 uA. The small improvement observed at the low stimulus frequencies is insignificant when compared with the huge shift seen at 10K and 15K Hz. Because this huge shift in the threshold for an electrically evoked cortical potential at 10K and 15K Hz after acoustic trauma was obtained, the possibility of current-induced fluid movement could not be ruled out.

An electric current applied within the cochlea may spread to other non-auditory structures. This spread would be a significant problem in the development of an electrical prosthesis. For this reason, the threshold of a cortical evoked response obtained off the auditory cortex was obtained. Since this cortical position would not be primarily innervated by auditory neurons and sound could not evoke a potential from this position, the thresholds would reflect the spread of stimulating current to other neural structures.

FIGURE 13

Thresholds for electrically stimulating the cochlea before and after acoustic trauma. Both of the stimulating electrodes were in the scala tympani of the basal turn. In order to damage the ear a +74 db, 1K Hz tone was presented for 30 min. After the presentation of this tone, sound could no longer evoke a cortical potential. Before the acoustic trauma, a -60 db, 15K Hz tone could evoke a response from the cortex.


GP 161 A
A8 L 10
BEFORE TRAUMA
AFTER TRAUMA
350
250
150
50
μA
300
500
1k
3k
5k
10k
30k
Frequency

Two threshold curves for an electrically evoked potential were obtained. One of these threshold curves was obtained at a cortical position from which an acoustically evoked potential was obtained. The second threshold curve was obtained at a cortical position which was insensitive to sound. Figure 14 illustrates the difference between these two threshold curves.

Below 3K Hz, only a small, 5db, difference was found between the two threshold curves. At the high frequencies, a substantial increase in the differences can be seen. This increase reflects the low threshold at the high frequencies. At low frequencies, a very small increase in current intensity would stimulate non-auditory structures.

In summary, electrical stimuli applied within the cochlea can evoke auditory cortical potentials. At low stimulus frequencies, current levels below 50 uA appear sufficient to trigger auditory activity. The low threshold was obtained whether the cochlea was intact or damaged. At high stimulus frequencies, current levels below 50 uA were sufficient to evoke a cortical potential only in the undamaged cochlea. Once the cochlea was damaged, the threshold for the evoked potential was much greater than 50 uA.

DISCUSSION

The unambiguous and consistent thresholds obtained for cortical evoked potentials indicated the existence of two auditory areas which were sensitive to low frequency acoustic stimuli. Between these two low frequency regions, the auditory cortex was generally responsive to the high frequencies. Although the present study supported Kayrers and Legouix (1963) in finding evidence for two low frequency regions, two differences between the studies emerge. While the high frequency auditory region joined the two low frequency regions in the present study, these low frequency areas were separated by an insensitive region as well as a high frequency region in Kayrers and Legouix study.

Both the present study and the earlier one used primarily the same method to identify the auditory areas. This method consists of the separation of auditory areas according to their sensitivity to the frequency of acoustic stimulation. Although this method has been often employed, other methods can be used to identify the various auditory regions.

Among the other means available, the latency of the evoked potential was also used in the present study. Evoked potentials from posterior positions on the cortex had longer latencies than potentials from anterior positions. These data suggest,along with the frequency data,that the auditory cortex should be divided into two regions - an anterior auditory area and a posterior auditory area.

Unfortunately, the latency data to click stimulation and the frequency threshold data to tonal pulses were collected in different

animals. The between-animal variability in the shape and location of the auditory cortex prevents a precise comparison of these two sets of data. However, the long latency cortical area appears to include the small posterior low frequency area. It also appears to include the portion of the high frequency area that lies in the posterolateral region of the auditory cortex.

The latency data of the present study, therefore, suggest that the small posterior low frequency area is a part of the same region as the high frequency area lying immediately lateral to it. So, while the present study indicates a posterior auditory area oriented in the medial-lateral direction, the earlier study by Kayrers and Legouix indicated an anterior-posterior orientation to the posterior area. With the medial-lateral orientation, the evoked potentials from the entire posterior auditory area would have identical latencies.

In the anterior-posterior organization, the low frequency portion of the posterior auditory area would have a long latency while the high frequency portion would have a short latency. Kayrers and Legouix did not report any latency data.

In the present study, the high frequency region extended to the anterior low frequency regions. The unresponsive region reported by Kayrers and Legouix was not found in the present study. Perhaps the use of 18 stimulus frequencies, in the present study, instead of the three used in the earlier study can account for this difference in the data. Since both the large high frequency regions and the anterior low frequency region had the same latency for evoked potentials,

these low and high frequency regions may be part of one auditory area.

By including latency data, the interpretation of the frequency data, in the present study was altered from that proposed by Kayrers and Legouix. Besides the latency and frequency data, other methodological approaches are yet to contribute to our understanding of the guinea pig auditory cortex. Ablation studies to show the various cortical regions are one type of investigation.

The demonstration of cortical-cortical connections through electrical stimulation of the cortex is a second type while degeneration at the thalamus after cortical ablations is still another. Each approach would offer new information about the guinea pig cortex, and each may modify, the organization that has been extrapolated from the frequency and latency data.

In spite of the fact that the present data firmly supports the existence of two tonotopic regions, additional auditory areas could be present. The data obtained from the guinea pig could be very similar to that obtained by Woolsey (1960, 1961) in the cat. In their pioneering study, Woolsey and Walzl (1942) did not clearly differentiate AII from Ep. These auditory areas were not clear from the data because the posterior ectosylvian sulcus obscured some of the evoked potentials in most animals. Therefore, Wolsey and Walzl interpreted their results as indicating only two auditory areas. This interpretation was in conflict with the cytoarchitecture studies of Rose (1949a, 1949b). Later experiments by Woolsey and

his students (Downman, Woolsey and Lende, 1960; Sendberg and Thompson 1962) clarified the interpretation of the evoked response data. AII was clearly separated from Ep yielding a total of three cortical areas each of which was shown to have a complete representation of the cochlea.

A similar development may occur with our understanding of the auditory cortex of the guinea pig. Although the guinea pig cortex does not have sulci to hinder neurophysiological studies, its small size may pose formidable problems.In a small cortex, radiation of evoked activity from one area to the next may obscure the location of these neighboring regions. So,future evidence may indicate that what now is believed to be a single area may actually be two auditory regions. A hint that this may be the case is found in the present data. Data from individual guinea pigs show an orderly progression of best frequencies along the lateral border of the auditory cortex. This progression was found in all animals (see the Appendix). These data suggest,but only suggest,that a third tonotopic area could lie along the lateral border of the auditory cortex.

Although the present data does not establish the existence of a third tonotopic area beyond any doubt, the suggestion of such an area must be taken seriously. After Downman, Woolsey and Lende (1960) firmly established the separate existence of AII and Ep in the cat, Woolsey was able to find data in his earlier studies which supported the separate existence of these auditory regions.

The data of the present study presents a picture very similar to the one presented by Woolsey and Walzl. A third tonotopic area is suggested; however, the data needed to establish this area's existence has not been obtained.

Recently the concept of tonotopic organization has been questioned. Single cell studies of the cat auditory cortex have not found the orderly data that had been obtained with gross evoked potentials. For example, Evans and Whitfield (1964) and Evans, Ross and Whitfield (1965) studied units in the unanesthetized primary cortex of the cat. The correlation between the best frequency of a unit and the position of that unit on the auditory cortex was very low. A unit with a best frequency of 10K Hz could be found anywhere between 7 and 14 mm rostral to the external meatus. This range covered approximately 90% of the auditory cortex. Goldstein et al (1970) reported similar evidence also in the cat. On the other hand, when using a lightly anesthetized cat, Hind et al (1960) found better agreement than in these other studies between a unit's best frequency and its position on the auditory cortex. However, even in Hind's study, the tonotopic arrangement was not compelling.

Although data obtained from single unit studies have not substantiated the evoked potential data, the organization that is generally accepted for the auditory cortex rests on the gross evoked potentials. However, a discrepancy does exist in the cat, the removal of which would enhance the confidence in the accepted organization of a central area surrounded by a peripheral belt.

Certain methodological differences between evoked potential studies and unit studies may have contributed to this discrepancy. Among these methodological differences are the level of anesthesia and the method of stimulation. With the exception of Hind (1960), all unit studies mentioned have used an unanesthetized preparation. Hind had used "lightly anesthetized" cats. Studies employing the gross evoked potential, on the other hand, have used very deep anesthetic levels. This difference in anesthetic levels may be the cause for the discrepancy of the evoked potential and the single unit data.

In the unanesthetized state, neurons in the auditory cortex may respond to very complex features of the acoustic input. Anesthesia may depress some of the cortical activity and thereby reveal the underlying tonotopic organization. Unfortunately, anesthesia also suppresses unit activity so that the tonotopic organization can be viewed only by using evoked potentials. Under this hypothetical explanation of the discrepancy between the evoked potential and single unit data, the organization revealed with evoked potential recording is masked by spurious unit activity in the unanesthetized state. This suggestion is supported by Hind's (1960) study. Light anesthesia was used in Hind's study which revealed the clearest tonotopic organization or units.

Besides differences in anesthesia, the unit and evoked potential studies differed in the method used to stimulate the auditory system. All the unit studies have used tonal stimuli. Evans and Whitfield (1964) and Evans, Ross and Whitefield (1965) used continuous

pure tones. Goldstein et al (1970) and Hind et al (1960) used tonal pulses. Woolsey and his students, on the other hand, did not use a sound stimulus at all. They electrically stimulated restricted portions of the spiral lamina. In their method, the bone of the cochlea was fractured allowing the cochlear fluids to drain. Therefore, the spread of the electrical stimulus should have been minimal. On the other hand, sound stimulates very large portions of the basilar membrane. As Johnstone's (1970) recent study has shown, acoustic stimuli of low frequency produce almost the same amount of movement in the basal portion of the basilar membrane as sounds of high frequency. Therefore, sound, as used in the unit studies, stimulates large portions of the basilar membrane; electrical pulses, as used in Woolsey's laboratory, stimulate restricted portions of the basilar membrane. These gross differences in the form of stimulation could account for the differences in the data.

Tunturi also found convincing evidence of tonotopic orangization in the dog. However, unlike Woolsey, Tunturi used acoustic stimuli in his investigations. In his pioneering study, Tunturi (1944) used tonal pulses and simply recorded gross evoked potentials from the cortex. His data suggested a tonotopic organization but the boundaries of responsive areas showed a very large amount of overlap. When Tunture (1950) in later studies applied strychnine to the cortex, the tonotopic organization became more apparent. Hind (1953) also used strychnine in an investigation of the auditory area of the cat.

Although the reason that the strychnine method produces such orderly data is not clear, one can imagine that strychnine accentuates any difference in the stimulation that sounds of various frequencies have on the basilar membrane. Most acoustic stimuli produce movement over very large portions of the basilar membrane; however, each frequency produces its maximum at a specific point.

If points on the basilar membrane are connected to points on the cortex, as Woolsey's work suggest, small differences in the movement of regions along the basilar membrane may be reflected by small differences in activity all the way to the cortex. Strychnine then could enhance these differences.

In recent studies, Tunturi (1955) was able to demonstrate a very orderly tonotopic organization without the use of strychnine. In these studies, Tunturi used the elementary pulse of Gabor. This sound pulse has two special features. It has a very limited frequency spectrum and it is very short (about 5 cycles). Von Bekesy (1955) using his model of the basilar membrane with neural supply, has shown that stimuli with short durations are perceived as being applied to a smaller area of the skin than stimuli with long durations. Therefore, the physical brevity as well as spectral restrictiveness of Tunturi's stimuli would tend to limit it to a restricted number of auditory fibers. For this readon, the elementary pulse of Gabor may be analogous to electrical stimulation of the spiral lamina and a good tonotopic organization obtained.

The method of stimulation and recording used in the present study was very similar to Tunturi's first map of the dog. Tonal pulses stimulated the ear; gross evoked potentials were recorded from a non-strychnized cortex. The pattern of results found in the present study was also very similar to Tunturi's results. In both studies, the data clearly indicated a tonotopic organization. However, the organization seen in either study was not as crisp as that seen when either strychnine was applied to the cortex or stimulation was severely restricted to a portion of the auditory nerve. On the other hand, the data obtained in the present study showed better organization than found in single unit studies.

Up to this point, the response of the auditory cortex to tones of different frequencies has been considered. Now, the effect of the intensity of the tonal pulse will be discussed. As mentioned in the introduction, the intensity function of the cochlear potential has been known for a long time. As the maximum amplitude of this function is approached, both the odd and the even harmonics of the stimulating frequency can be recorded in the cochlear potential. Since some of the acoustic energy is dissipated in the production of these harmonics within the cochlea, the intensity function departs from linearity. Once the maximum is reached, further increases in the sound intensity reduce the amplitude of the cochlear potential. This reduction is seen not only at the fundamental frequency but also at its harmonics. Therefore, at these very high sound intensities, the acoustic energy is no longer being efficiently transduced into the

cochlear potential. Since a smaller percentage of the acoustic energy is being used to produce the cochlear potential, some of the energy imparted to the cochlea must be dissipated as heat or as mechanical movement unrelated to the production of the cochlear potential.

The data of this study indicate that very intense sounds are not only inefficient in the production of the cochlear potentials, these intense sounds are also inefficient in producing neural activity. At high stimulus intensity,a larger amount of acoustic energy produces a lower amplitude evoked cortical potential. Because of the similarity of the two intensity functions, the inference that the cochlear potential is related in a causal manner to the initiation of the neural activity is tempting. However, as in the case of any correlation, causality cannot be strictly inferred. The data do not contradict a causal hypothesis. If the evoked cortical potential had not decreased when the cochlear potential decreased,then a contradiction would have been obtained.

Although the amplitude of the evoked potential was related to the intensity of the sound, the present experiment did not study the coding of loudness as such. The increase in neural activity with increases in the intensity of the sound may indeed code for loudness. On the other hand, this increase in neural activity may be totally unrelated to that code.

For the data discussed in the previous sections, sound was used to stimulate the auditory system. Now, data obtained by electrically stimulating the cochlea will be discussed.

The lowest current thresholds were obtained when both stimulating electrodes were in the scala tympani of the basal turn. This electrode placement was more efficient than any other electrode placement. The efficiency of the dual scala tympani placement can be predicted from the electrical impedance characteristics of the cochlea.

In the introduction, these impedance characteristics have been described. Both the basilar membrane and Reissner's membrane appear to be highly resistant to the passage of electrical current. When one stimulating electrode is in the scala tympani and the other electrode is in scala vestibuli, the major current path would be through the helicotrema. This path through the helicotrema would be many times longer than the path between two electrodes in the scala tympani. Since the extended length of the current path through the helicotrema would offer a larger area of surrounding tissue through which a portion of the stimulus would be shunted, the long path should show a higher current threshold than a short path.

When both stimulating electrodes were in the scala tympani of the basal turn, the threshold for an electrically evoked potential at 10K Hz was below 45 uA. However, this low threshold value depended upon the cochlea being intact. After substantial acoustic trauma, the threshold for a 10K Hz electrical stimulus was elevated to over 350 uA. On the other hand, electrical stimuli lower than 1K Hz had a threshold below 45 uA both before and after acoustic trauma.

The major effect of acoustic trauma is the destruction of the sensory hair cells. Although the auditory nerve fibers may subsequently degenerate, this degeneration would need several months to occur. Since the threshold for a 10K Hz electrical stimulus was elevated by acoustic trauma, the low pre-trauma threshold probably depended upon intact hair cells. The low intensity 10K Hz stimulus could have depolarized the hair cells but could have been unable to depolarize the nerve fibers until the intensity was raised. On the other hand, a 10K Hz stimulus might cause movement in the cochlear fluid. An intact ear would respond to such movement in the same way it responds to sound. In any case, the low threshold for a 10K Hz electrical stimulus seems to depend upon intact hair cells while the low threshold for a 1K Hz stimulus does not seem dependent upon these hair cells.

When the electrical stimulus was just above threshold, it evoked a cortical potential that had a very large amplitude. Often a 1 mv peak to peak evoked potential was recorded from a just supra-threshold electrical stimulus. If the electrical stimulus was reduced 4 db, the evoked potential disappeared entirely.

In the acoustical situation,a very different picture was obtained. If the sound intensity sufficient to produce a 1000 u volt potential was reduced,the potential was proportionally reduced and did not disappear. In the electtical situation the stimulus range from threshold to maximum response was only 4 db! In the acoustical situation the range was more like 40 to 60 db.

These data suggest that a just suprathreshold electrical stimulus may sound very loud. As in a recruiting ear, there is an abnormally rapid rise in loudness as the stimulus intensity is increased. This recruitment-like phenomenon would be a significant problem in the development of an electrical prosthesis for the ear.

In the introduction, a number of animal behavioral studies in which subcortical auditory structures were electrically stimulated have been reviewed (Neider & Neff 1901; Gerkin 1965, 1970). In these studies, the animals were trained to respond either to an acoustical or to an electrical stimulus. In a number of cases after the task was learned, the animal was tested to see whether or not the training transferred to the other mode of stimulation. If electrical stimulation and acoustical stimulation produced the identical percepts, complete transfer in both directions would be expected. In Neider's study, transfer from the acoustic stimulus to electrical stimulation (of the inferior colliculus) was good. Transfer in the opposite direction was poor. In Gerken's study, only transfer from electrical stimulations to acoustical stimulation was tested. The, transfer was poor. So while transfer from an acoustical stimulus to an electrical stimulus was good, the transfer from electrical to acoustical was poor.

This asymmetry of transfer effects may be explained by the intensity data obtained in the present study. These data suggest that an electrical stimulus might be perceived as a very loud sound.

Moreover, an electrical stimulus could easily involve non-auditory structures. Since Neider and Gerkin used acoustic stimulus of moderate intensities, the change from acoustical to electrical stimulation might involve an increase in stimulus intensity. This increase in the stimulus may make transfer of learning easy. On the other hand, switching from an electrical stimulus to an acoustical stimulus might reduce the stimulus intensity. This reduction might make the transfer of learning more difficult. Moreover, the transfer seen in the behavioral data may be a result not of learning but of only sensitization. This contention has been developed in the introduction. Since an intense stimulus was used, the asymmetry of transfer can also be explained if the sensitization accounts for the observed transfer.

The data of the present study suggest that loud sounds should be used, at least initially, when transfer effects between electrical and acoustical stimuli are tested. With loud sounds, the differences between the two modes of stimulation would be minimum. If the electrical stimulus was carefully restricted to auditory structures, transfer of learning in both directions should be observed.

Moreover, the data suggest that the electrical stimuli employed in this study are less than optimal. New methods for applying the electrical stimulus may make the cortical intensity functions evoked by electrical stimulation similar to the intensity

functions evoked by acoustic stimulation. The recruitment-like phenomenon observed in the present study must be eliminated before a successful prosthetic device is developed.

In summary, electrical stimulation of the cochlea can be accomplished without acute injury to the inner ear. Current thresholds for a cortical evoked potential tend to be below 50 uA. Placement of both stimulating electrodes in the scala tympani appeared to be most efficient for the stimulation of the auditory system. Finally, a just suprathreshold stimulus appeared to produce a very large evoked potential. This large potential may indicate that a just suprathreshold stimulus may sound very loud.

SUMMARY AND CONCLUSIONS

Auditory Cortex of the Guinea Pig

The results of an earlier mapping study, by Kayrers and Legouix, had been extended. In that study, two tonotopic areas were found. While one of these areas responded to each of the three stimulus frequencies used, the other area responded only to the low and moderate frequencies. Since only three frequencies were used in the earlier study, the present study made a more complete map using 18 stimulus frequencies. The present data support the existence of the two areas previously reported. However, both areas appear to respond to both low and high stimulus frequencies. The data also suggest the possible existence of a third auditory area.

Intensity Function of the Cochlea and Cortex

Amplitude changes of the cochlear potential due to increases in sound intensity were compared in the same animals with amplitude changes in the evoked potential from the cortex. As is well known, the cochlear potential is linear over a 30-50 db range. Above this linear region, the cochlear potential departs from linearity and plateaus. Further increases in the sound intensity reduce the amplitude of the cochlear potential. The cortical-evoked potential behaves in a similar manner. The amplitude of the cortical-evoked potential increases with increases in sound intensity as long as the response of the cochlea is linear. When the cochlear potential departs from linearity, the increases in the evoked potential also tend to plateau. At the point the

cochlear potential decreases in response to an increase in sound, the evoked potential from the cortex also decreases. Therefore, the upper limit of intensities to which the cochlear potential responds with an increase in amplitude appears to be reflected in the gross neural activity as measured by the evoked potential.

Electrical Stimulation of the Auditory System.

A number of observations concerning the development of an electrical prosthetic device for the hard of hearing were made. The studies showed that electrodes could be implanted in the cochlea and thresholds to electrical stimulation obtained without acute damage to the inner ear.

By recording the evoked potential from the auditory cortex the threshold for electrical stimulation of the auditory system was estimated. Current thresholds were usually between 10 and 100 uA.

As stimulus intensity is increased, current spread from intracochlear electrodes would involve the vestibular nerve, the facial nerve, and other portions of the nervous system. By recording the cortical-evoked potential from a non-auditory area, the threshold for electrically stimulating other structures by the spread of current was estimated. The data suggest only a small intensity difference separates the threshold for stimulation of the auditory nerve and the stimulation of adjacent nerves. Often the measured difference was only 10 db. This spread of current will be a significant problem in developing an electrical prosthetic device.

An interesting phenomenon was observed, when the two stimulating electrodes were placed in the scala tympani of the basal turn. In this case, the thresholds for a 10K Hz stimulus was very low, under 50 uA. After the ear was damaged by acoustic trauma, the threshold for a 10K Hz electrical stimulus was raised to over 350 uA. This observation suggests that high frequency electrical stimuli may produce movement in the cochlear fluids.

The lowest thresholds for an electrically evoked cortical potential were obtained with both electrodes in the scala tympani of the basal turn. When the stimulating electrodes spanned the cochlear partition, as the case when one electrode was in scala tympani and the other in scala vestibuli, the current thresholds were very high. These data agree with experimental evidence which indicates that the cochlear partition is a good electrical insulator.

REFERENCES

Aran, J. M. Patterns of human electrocochleographic responses - Normal and pathological, Paper given at the 80th Meeting of the Acoustical Society of America, Houston, November 1970.

von Bekesy, G. The coarse pattern of the electrical resistance in the cochlea of the guinea pig (electro-anatomy of the cochlea) J. Acoust. Soc. Amer. 1951, 23, 18-28.

von Bekesy, G. Human skin perception of traviling waves similar to those on the cochlea, J. Acoust. Soc. Amer. 1955, 27, 155-161.

Choo, Y. B. and Tabowitz, D. The formation and flow of the cochlear fluids: II Studies with radioactive potassium (K^{42}), Ann. Otol, 1965, 74, 140-145.

Clark, G. M. Response of cells in the superior olivary complex of the cat to electrical stimulation of the auditory nerve, Experimental Neurology, 1969, 24, 124-136.

Coats, A. C. Human auditory-nerve action potentials and cochlear microphonics recorded nonsurgically, Paper given at the 80th meeting of the Acoustical Society of America, Houston, November 1970.

Davis, H. Biophysics and physiology of the inner ear, Physiol. Rev. 1957, 37, 1-49.

Davis, H. and Zerlin, S. Acoustic relations of the human vertex potential, J. Acoust. Soc. Amer. 1966, 39, 109-116.

Downman, C. B., Woolsey, C. N., and Lende, R. A. Auditory areas I, II, and Ep, cochlear representation, afferent paths and interconnections, Bull. Johns Hopkins Hosp. 1960, 106, 127-142.

Evans, E. F. and Whitfield, I. C. Classification of unit responses in the auditory cortex of the unanaisthetized and unrestrained cat, J. Physiol. 1964, 171, 476-493,

Evans, E. F. Ross, H. F. and Whitfield, I. C. The spatial distribution of unit characteristics frequency in the primary auditory cortex of the cat, J. Physiol. 1965, 179, 238-247.

Geddes, L. A. and Baker, L. E. Principles of Applied Biomedical Instrumentation, John Wiley & Sons Inc. New York, 1968.

Gerken, G. M. Detection by the guinea pig of acoustic stimulation and of electrical stimulation of the brain, Perception and Psychophysics 1966, 1, 137-141.

Gerken, G. M. Electrical stimulation of the subcortical auditory system in behaving cat, Brain Research, 1970, 17, 483-497.

Goldstein, M. H. Jr. Abeles, M. Daly, R. L. and McIntosh, J. Functional architecture in cat primary auditory cortex: Tonotopic organization, J. Neurophysiol. 1970, 33, 188-197.

Hind, J. E. An electrophysiological determination of tonotopic organization in the auditory cortex of the cat, J. Neurophysiol. 1953, 16, 475-483.

Hind, J. E. Unit activity in the auditory cortex, in Rasmussen, G. L. and Windle, W. F. (Eds.) Neural Mechanisms of the Auditory and Vestibular Systems, Thomas, Springfield, 1960.

House, W. Electrical implants for hearing, Conference held at Stanford Medical School, December 1970.

Johnstone, B. M. Taylor, K. J. and Boyle, A. J. Mechanics of the guinea pig cochlea, J. Acoust. Soc. Amer. 1970, 47, 504-509.

Kayrers, D. and Legouix, J. P. Projections tonotopiques sur le cortex auditif du Cobaye, Comptes Rendes De La Societe de Biologie, 1963, 157, 2161-2164.

Kern, E. B. Cody, D. T. and Bickford, R. G. Neurogenic components of the averaged response evoked by clicks in guinea pigs, Mayo Clinic Proc. 1969, 44, 886-889.

Kern, E. B. Thane, R. C. and Bickford, R. G. Vertex-response thresholds to pure tones in guinea pigs, Arch. Otol. 1969, 90, 315-325.

Kurokawa, S. Experimental study on electrical resistance of basilar membrane in guinea pig, Jap. J. Otol. Tokyo, 1965, 68, 1177-1195.

Licklider, J. C. R. Basic correlates of the auditory stimulus, in Stevens, S. S. (Ed.) Handbook of Experimental Psychology, John Wiley & Sons Inc. New York, 1951.

Mast, T. E. Binaural interaction and contralateral inhibition in dorsal cochlear nucleus of the chinchilla, J. Neurophysiol. 1970, 33, 108-115.

Michelson, R. The response with permanently implanted cochlear electrodes in sensory deafness: A preliminary report, Paper given at the 75th annual meeting of the American Academy of Ophthalmology and Otolaryngology, Las Vagas, October, 1970.

Nakashima, T. Sullivan, M. J. Snow, J. B. Jr. and Suga, F. Sodium and potassium changes in inner ear fluids, Arch. Otol. 1970, 20, 1-6.

Nieder, P. C. and Neff, W. D. Auditory information from subcortical electrical stimulation in cats, Science, 1961, 133, 1010-1011.

Perl, E. R. and Casby J. U. Localization of cerebral electrical activity: The acoustic cortex of the cat, J. Neurophysiol. 1954, 17, 429-442.

Rauch, S. Kostlin, A. Schnieder, E. A. Arguments for the permeability of Reissner's membrane, Laryngoscope, 1963, 73, 135-147.

Rose, J. E. The cellular structure of the auditory region of the cat, J. Comp. Neurology, 1949, 91, 409-439.

Rose, J. E. and Woolsey, C. N. The relations of thalamic connections, cellular structure and evokable electrical activity in the auditory region of the cat, J. Comp. Neurology, 1949, 91, 441-466.

Simmons, F. B. Mongeon, C. J. Lewis, W. R. and Huntington, D. A. Electrical stimulation of acoustical nerve and inferior colliculus, Arch. Otol. 1964, 79, 559-567.

Simmons, F. B. Epley, J. M., Lummis, R. C, Guttman, N. Frishhoph, L. S. Harmon, L. D. and Zuricher, E. Aucitory nerve: Electrical stimulation in man, Science, 1965, 148, 104-106.

Simmons, F. B. Electrical stimulation of the auditory nerve in man, Arch. Otol. 1966, 84, 2-54.

Sindberg, R. M. and Thompson, R. F. Auditory response fields in ventral temporal and insular cortex of cat, J. Neurophysiol. 1962, 25, 21-28.

Tunturi, A. R. Audio frequency localization in the acoustic cortex of the dog, Amer. J. Physiol. 1944, 141, 397-403.

Tunturi, A. R. Physiological determination of the boundary of the acoustic area in the cerebral cortex of the dog, Amer. J. Physiol. 1950, 160, 395-401.

Tunturi, A. R. A difference in the representation of auditory signals for the left and right ears in the iso-frequency contours of the right middle ectosylvian auditory cortex of the dog, Amer. J. Physiol. 1952, 168, 712-727.

Tunturi, A. R. Analysis of cortical auditory responses with the probability pulse, Amer. J. Physiol. 1955, 181, 225-229.

Tunturi, A. R. Masking of cortical responses in middle ectosylvian auditory area of the dog, Amer. J. Physiol. 1956, 184, 321-328.

Tunturi, A. R. Anatomy and physiology of the auditory cortex, in Rasmussen, G. L. and Windle, W. F. (Eds.) Neural Mechanisms of the Auditory and Vestibular Systems, Thomas, Springfield, 1960.

Wever, E. G. Theory of Hearing, John Wiley & Sons Inc. New York, 1949.

Woolsey, C. N. and Walzl, E. M. Topical projection of nerve fibers from local regions of the cochlea to the cerebral cortex of the cat, Bull. Johns Hopkins Hosp. 1942, 71, 315-344.

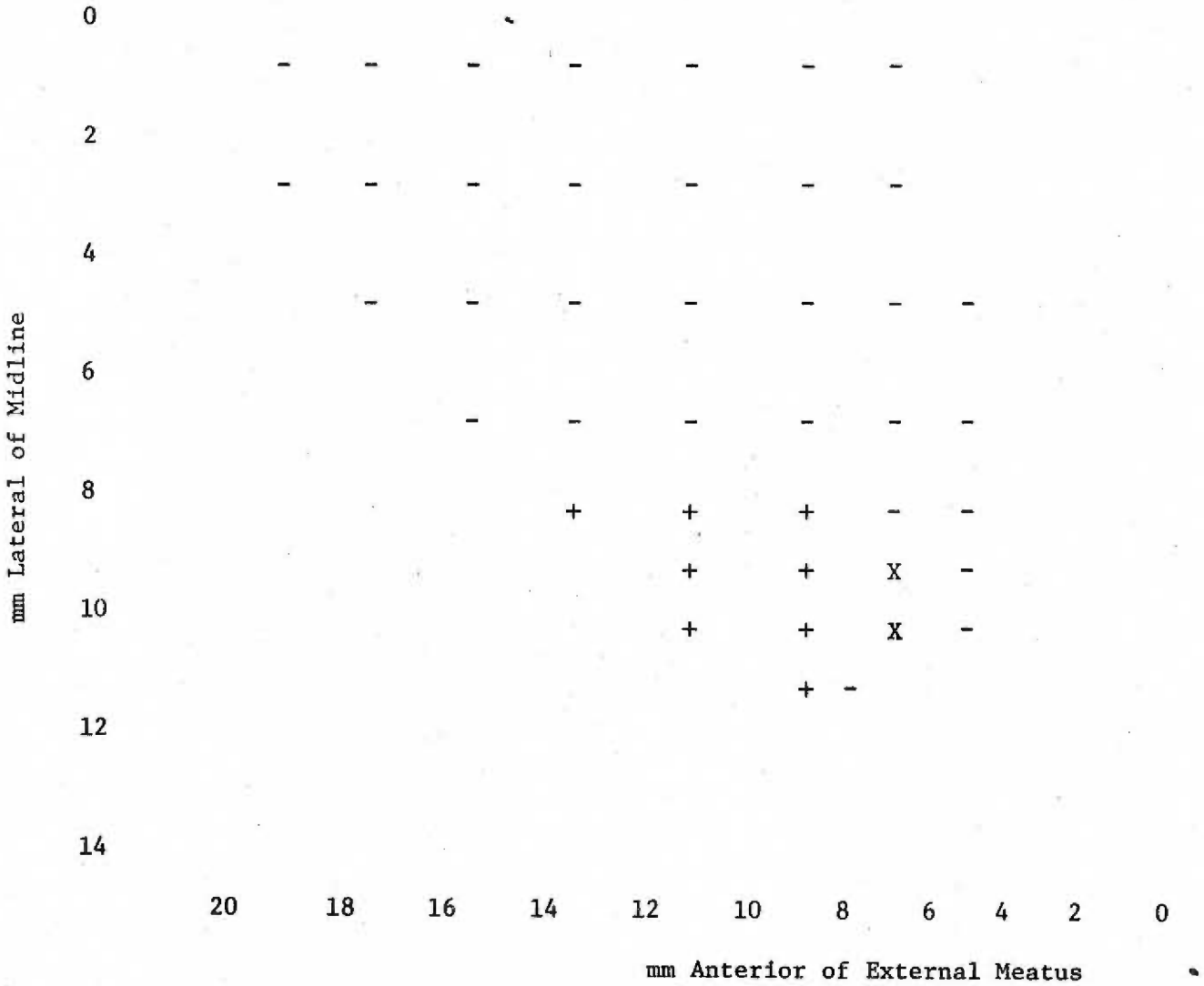
Woolsey, C. N. Organization of cortical auditory system: A review and a synthesis, in Rasmussen, G. L. and Windle, W. F. (Eds.) Neural Mechanisms of the Auditory and Vestibular Systems, Thomas, Springfield, 1960.

Woolsey, C. N. Orgnaization of cortical auditory system, in Rosenblith W. A. (Ed.) Sensory Communication, M. I. T. Press, Cambridge, 1961

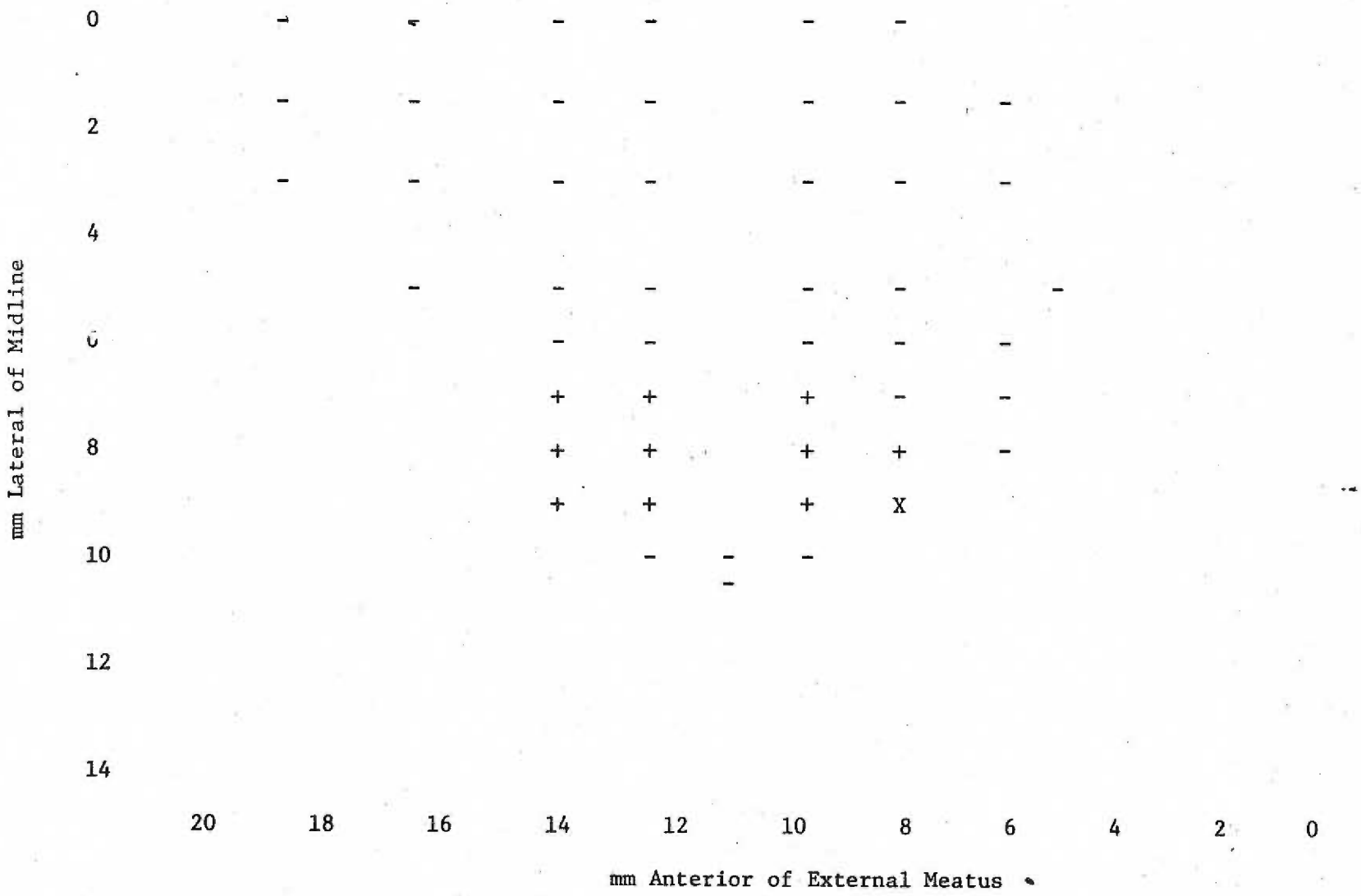
APPENDIX I

Positions on the cortex which were responsive to clicks. Areas from which a short latency response, 9-11 msec., was obtained are indicated by +, while areas from which a long latency response, 18-26 msec, was obtained is marked by X. Non-responsive regions are indicated by -.

Guinea Pig #75A



Guinea Pig #76A



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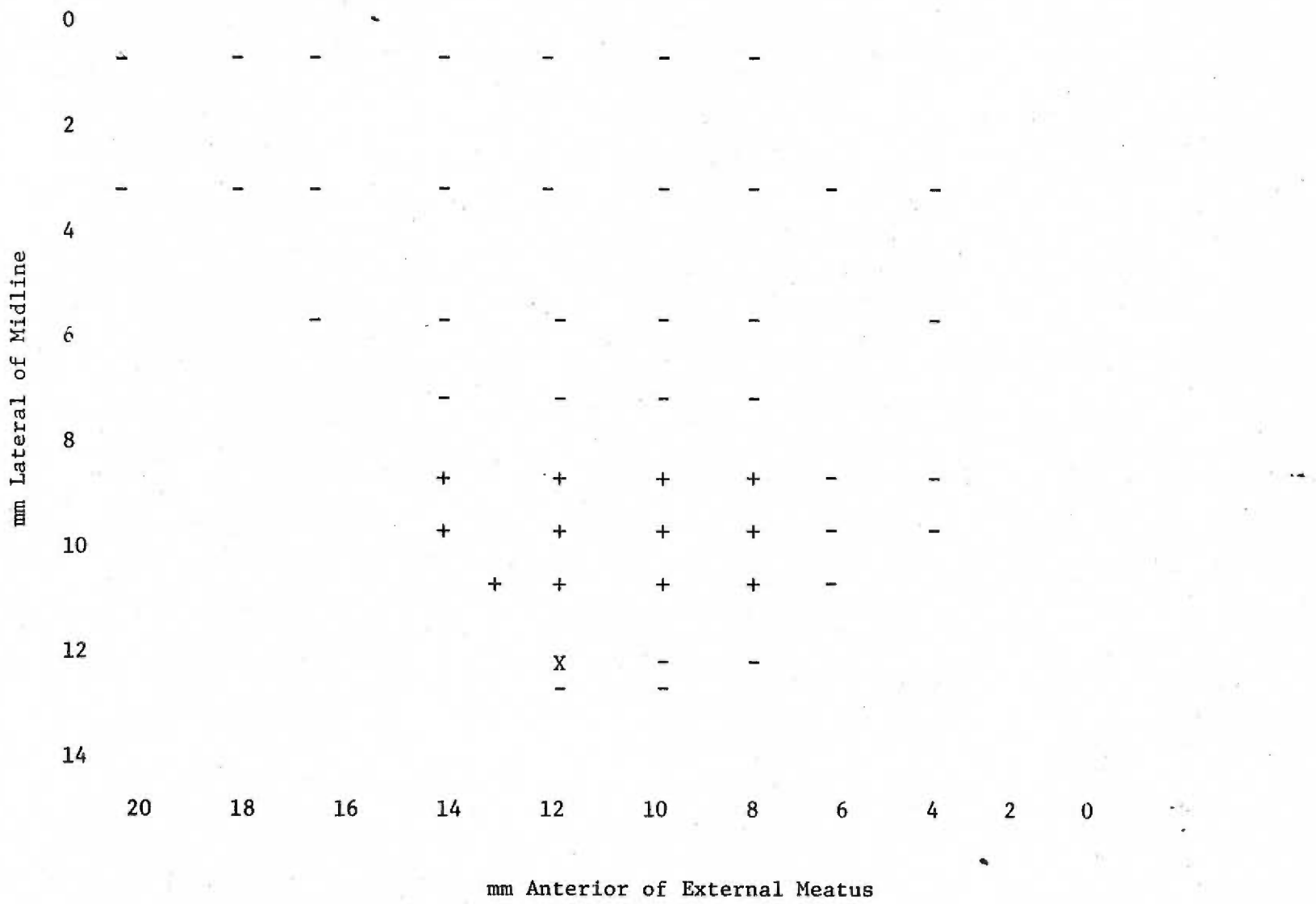

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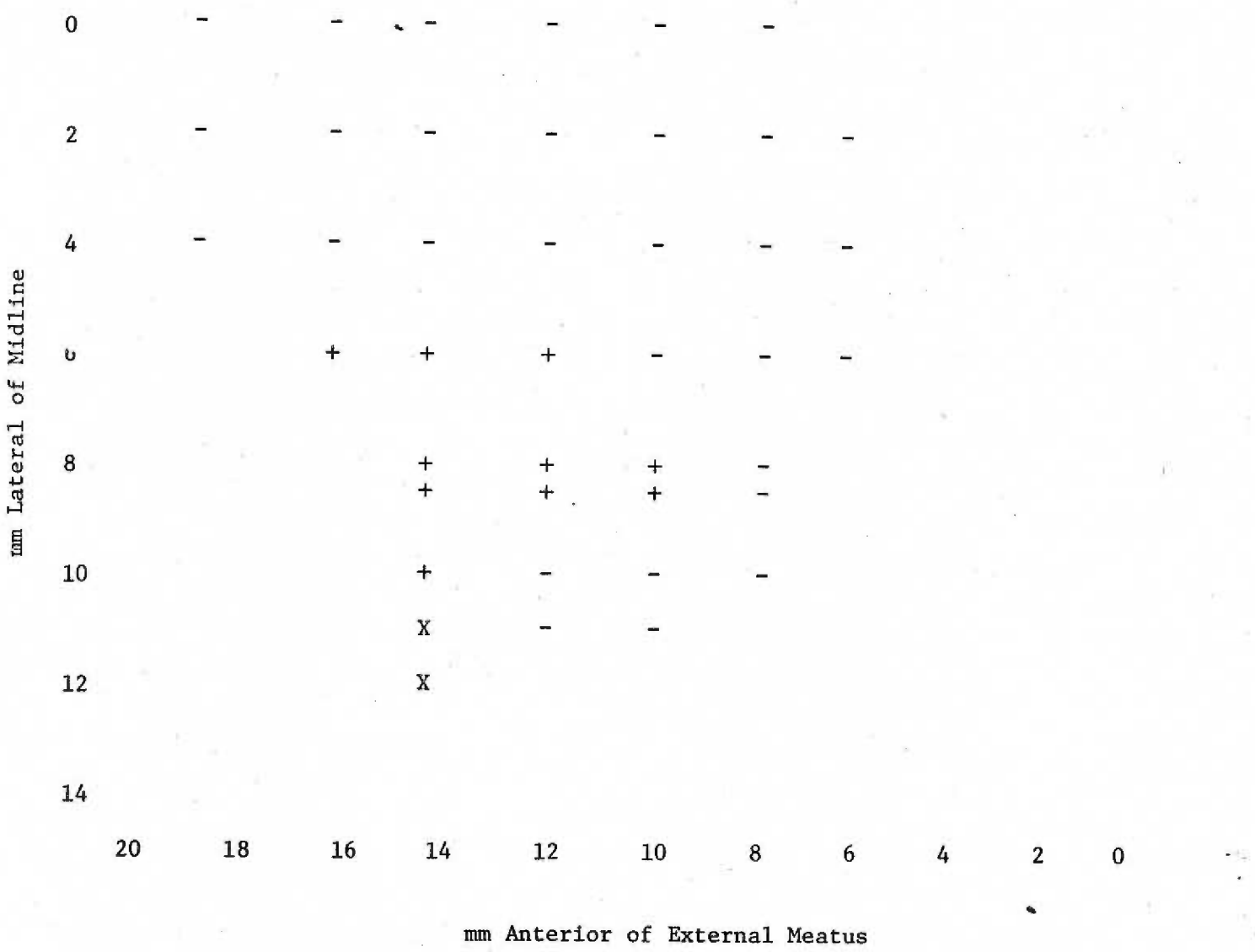
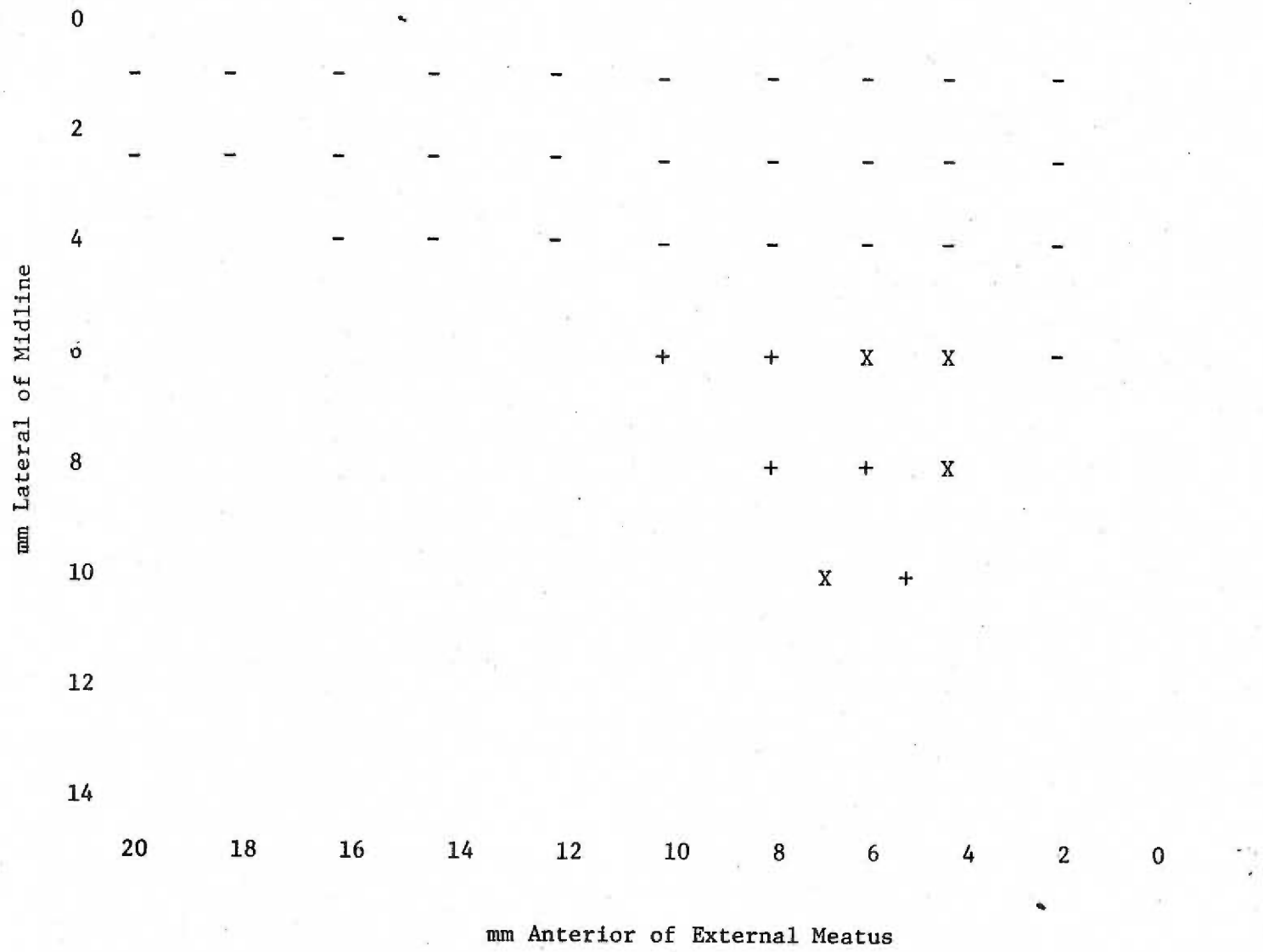
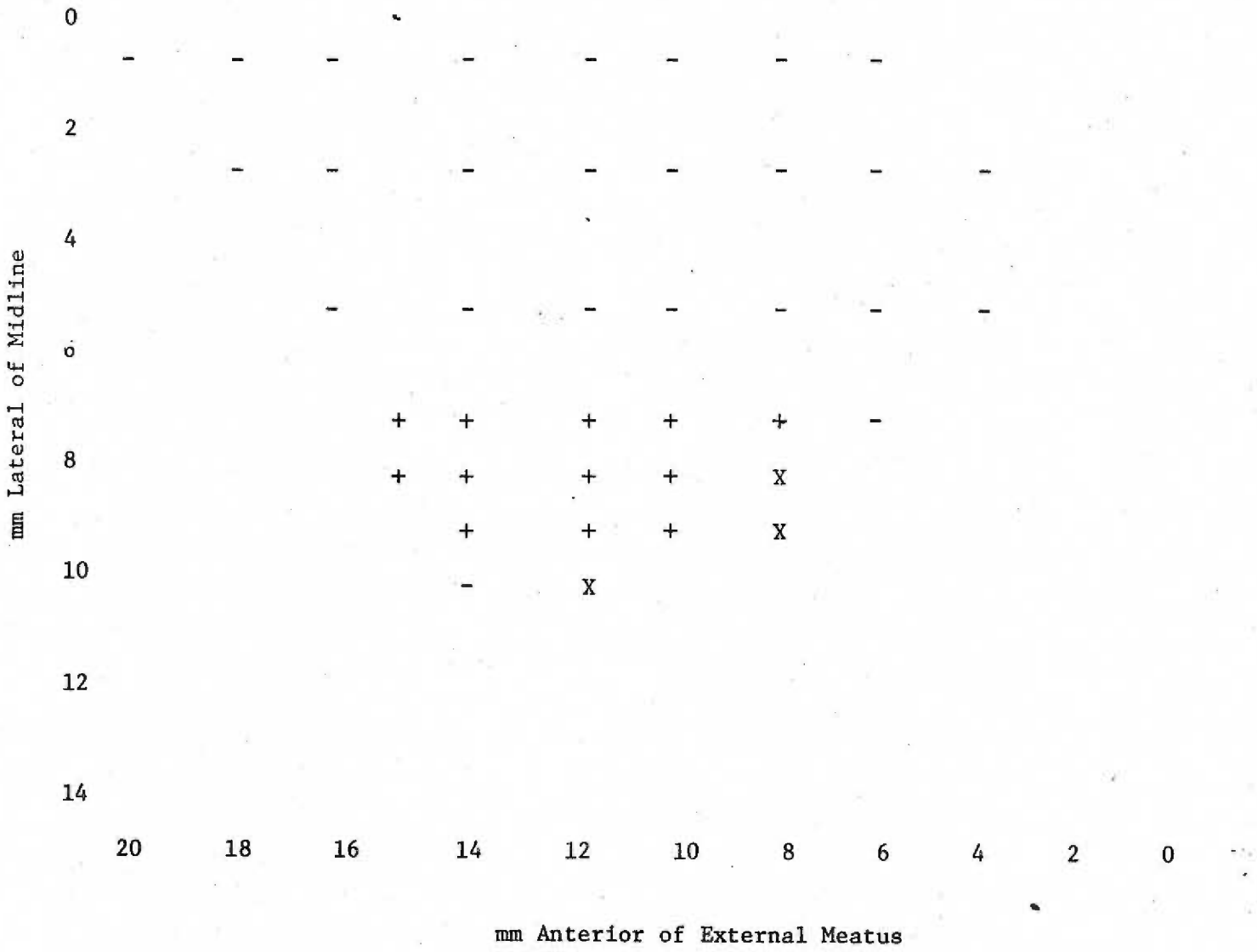


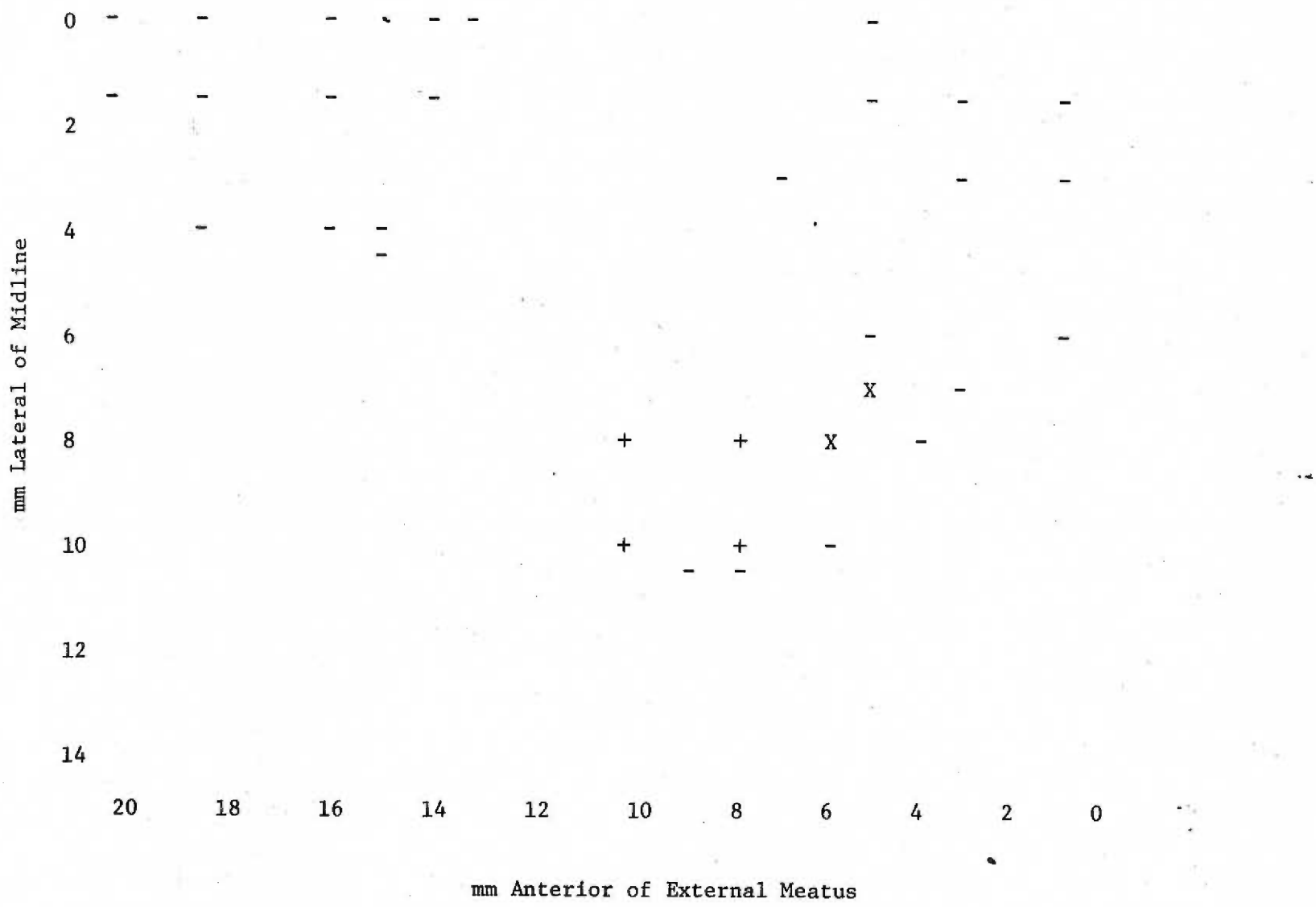
Guinea Pig #72



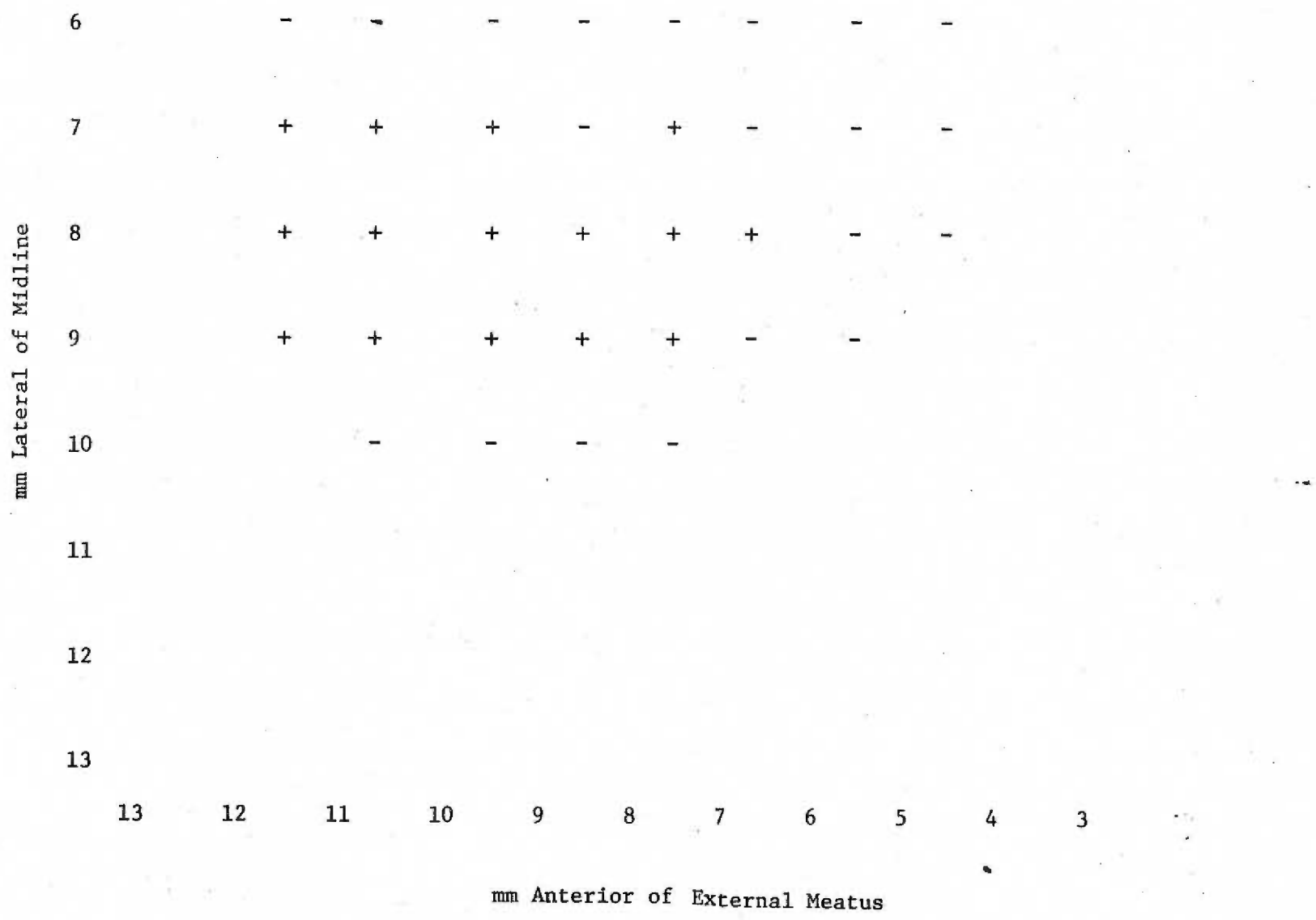
Guinea Pig #81A



Guinea Pig #73A



Guinea Pig #69A

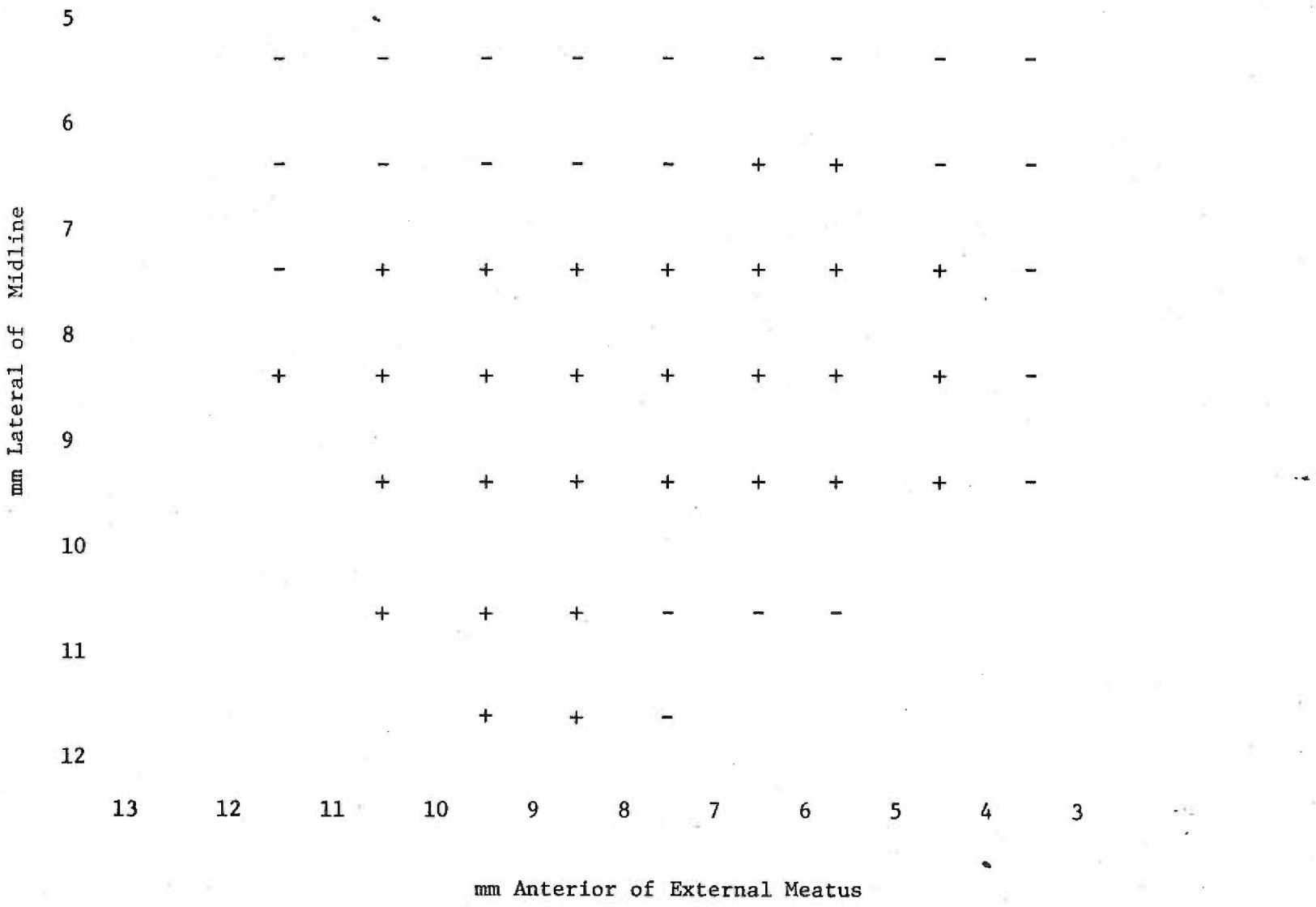


Guinea Pig #67A

mm Lateral of Midline	13	12	11	10	9	8	7	6	5	4	3
6	NR	S	S	S	S	S	S	NR	NR	NR	
7	NR	L	L	L	S	L	S	NR	NR	NR	
8			L	L	L	L	S	NR	NR	NR	
9			NR	S	L	L	S	S	S		
10				S	L	S	NR				
11				L	S						
12											
13											

mm Anterior of External Meatus

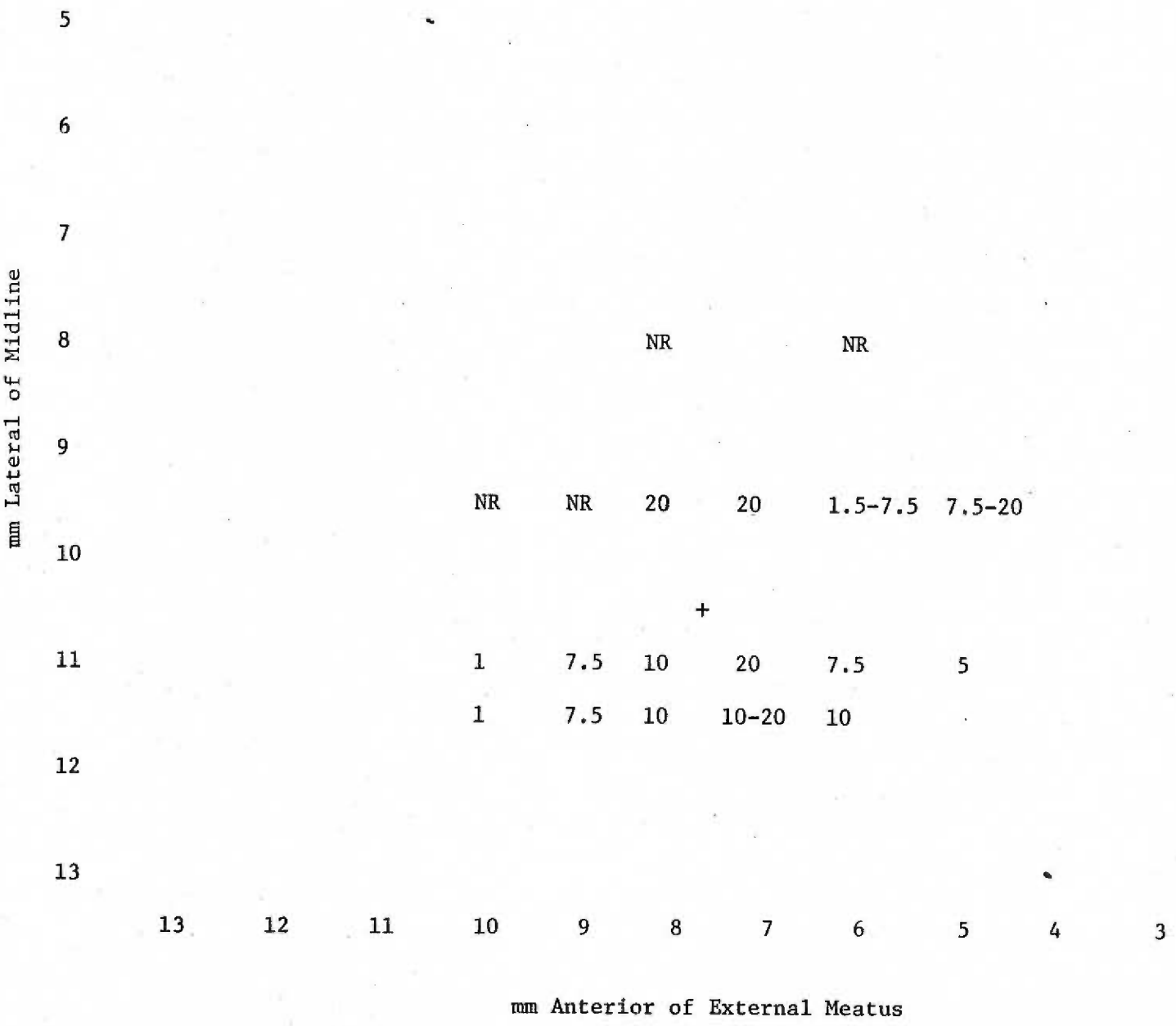
Guinea Pig # 69A



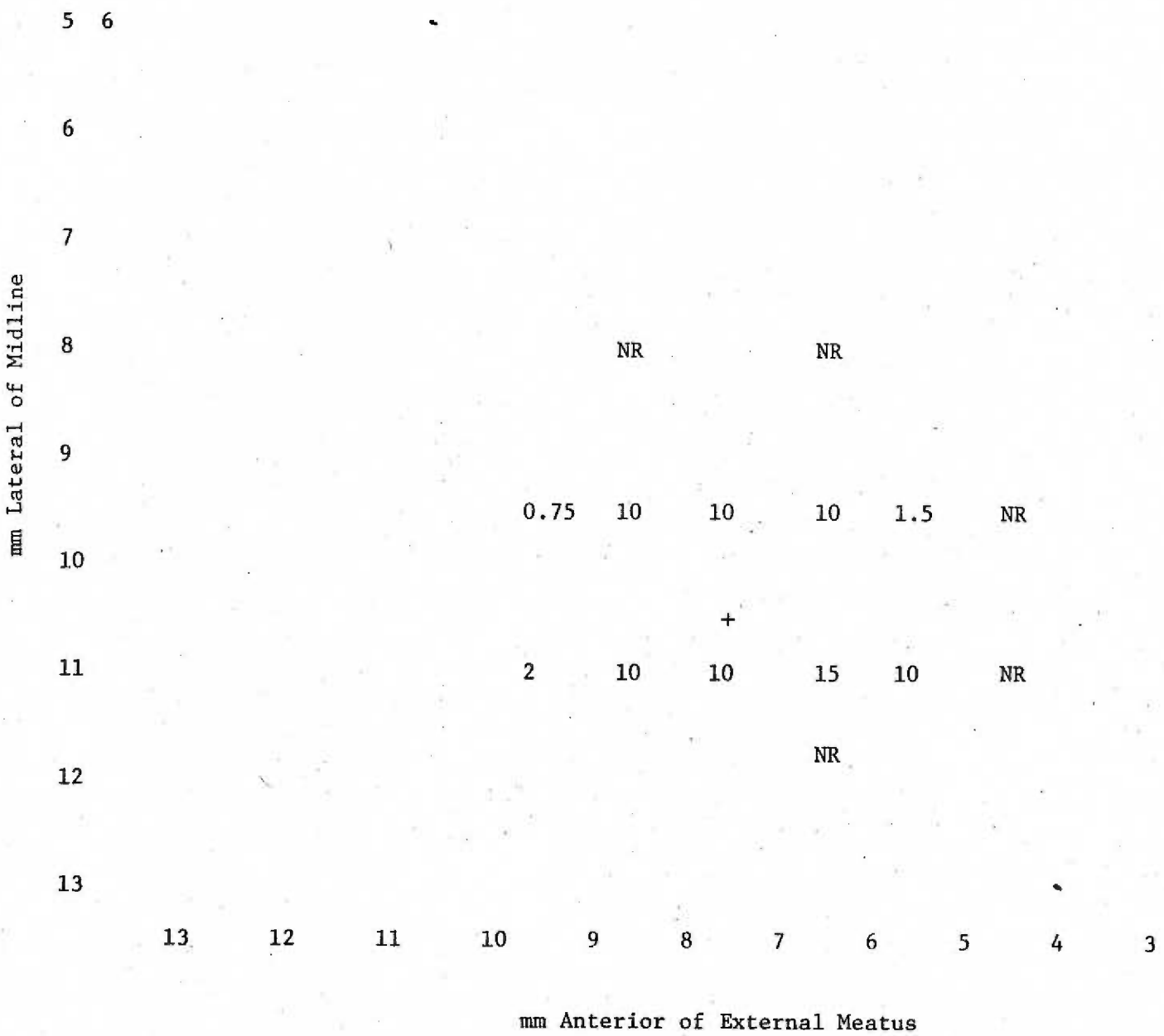
APPENDIX II

Detailed map of the auditory cortex of the guinea pig. The numbers represent the best frequency at that position in kilohertz. Non-responsive areas are indicated by NR. The approximate center of the auditory area is marked by +.

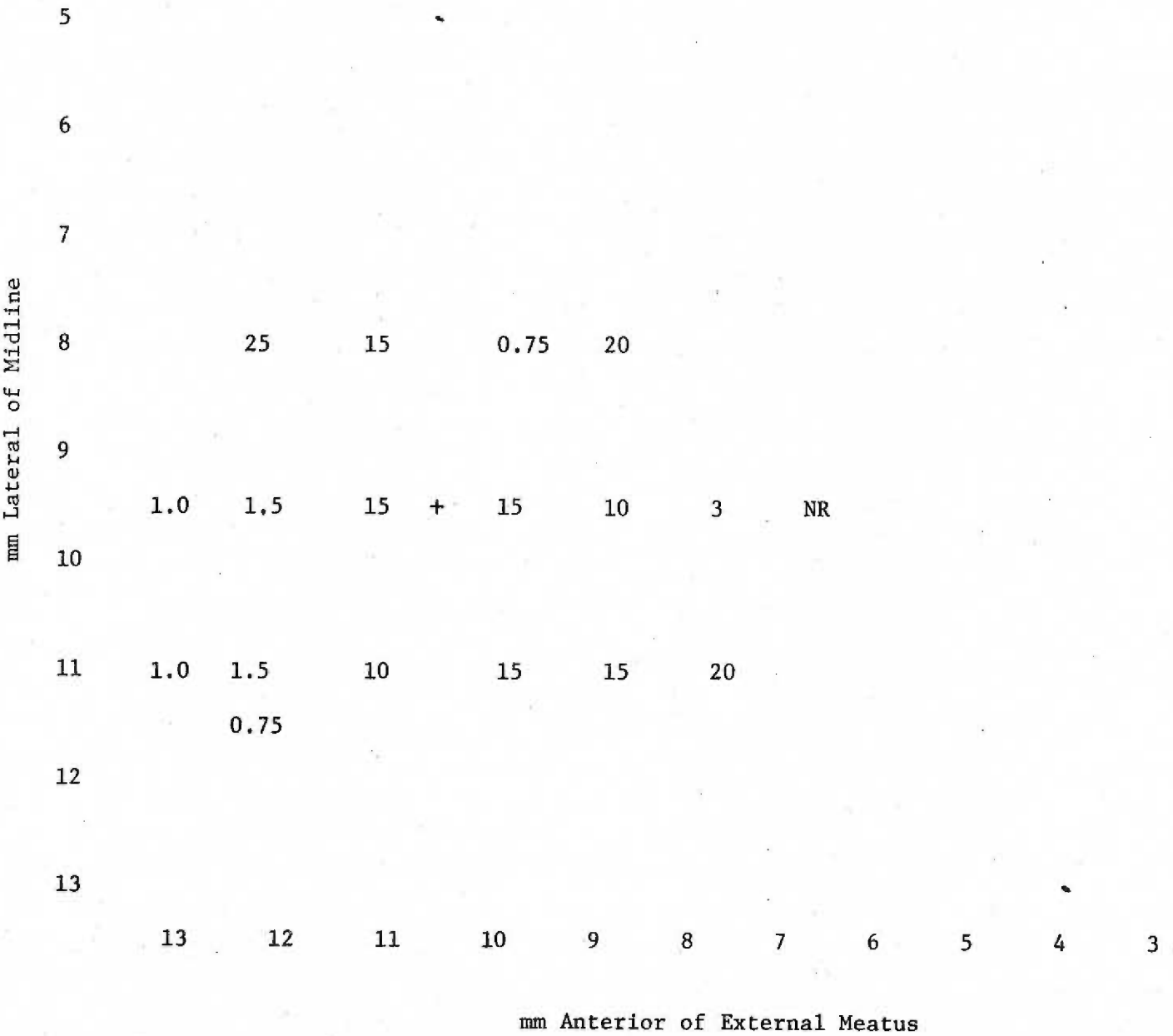
Guinea Pig #102A



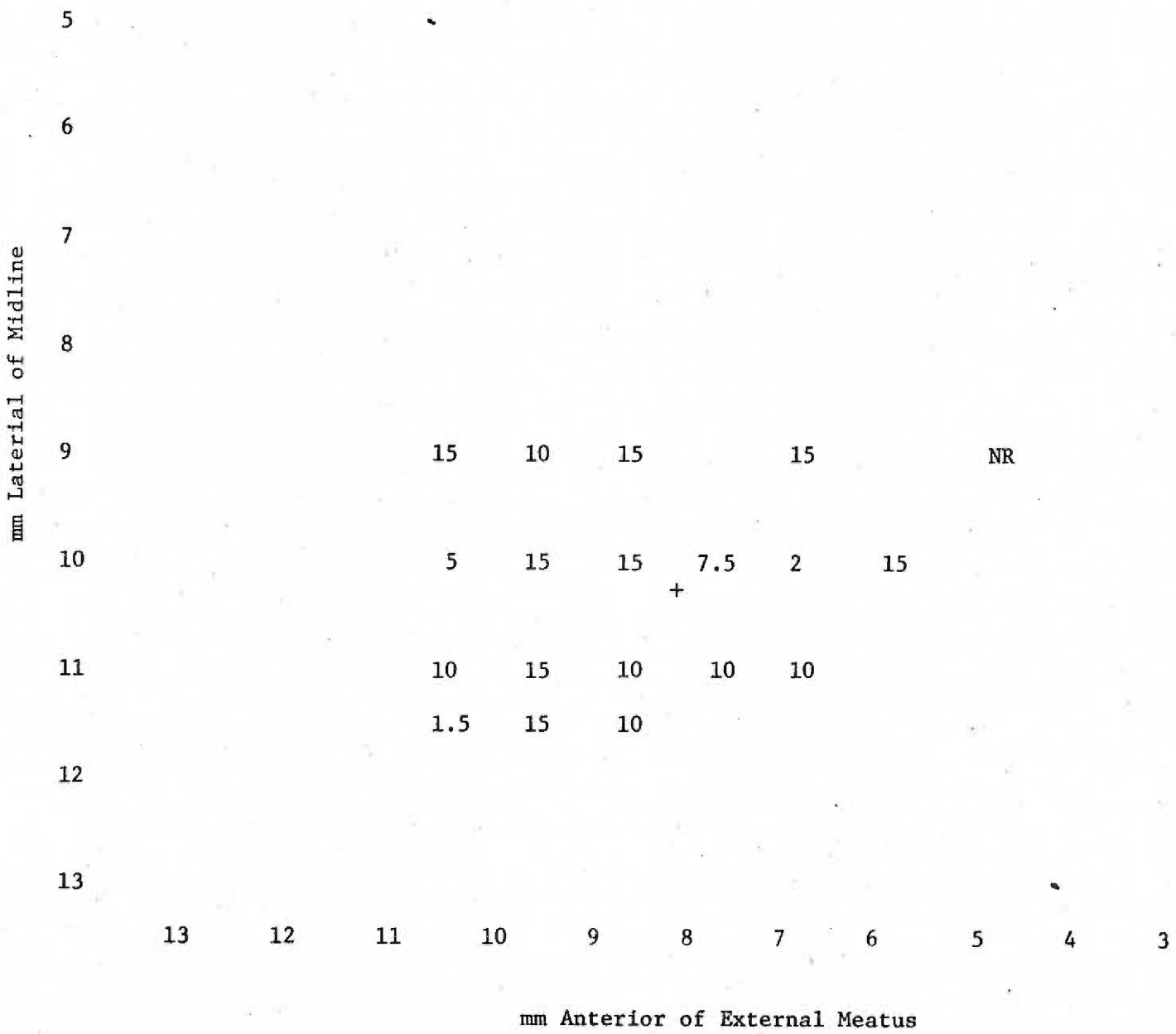
Guinea Pig #103A



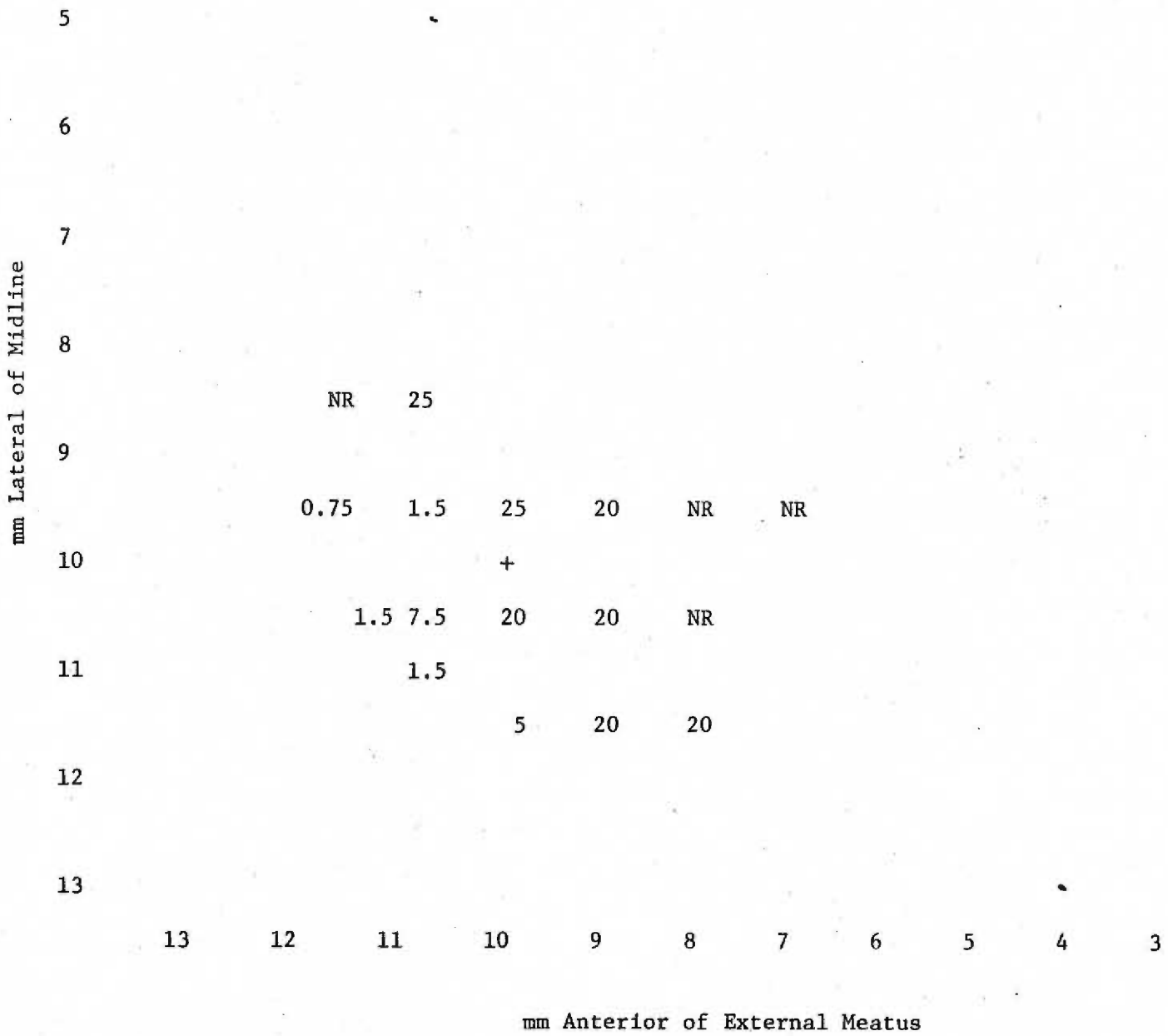
Guinea Pig #92A



Guinea Pig #90A



Guinea Pig #97A

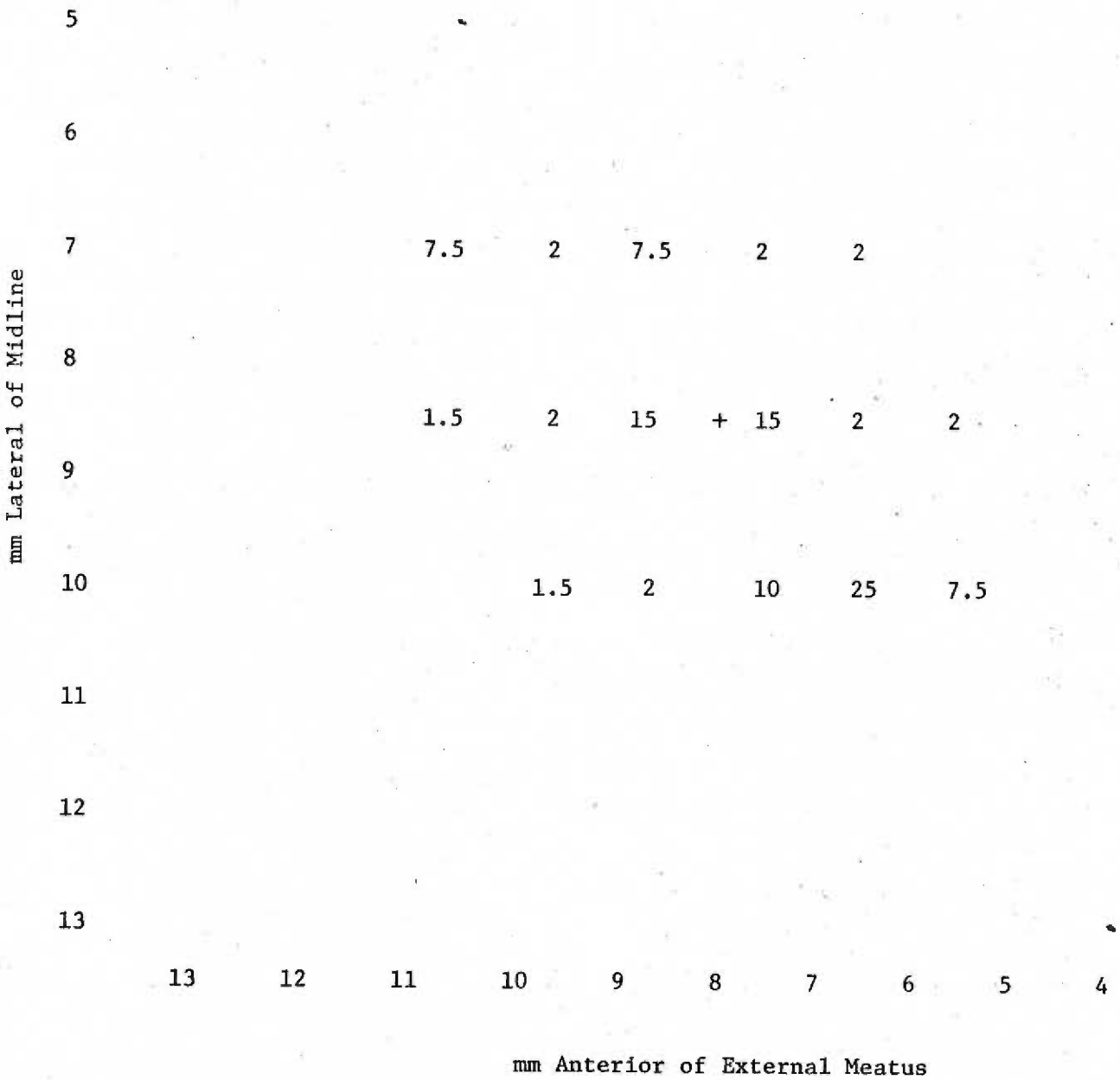


Guinea Pig #104A

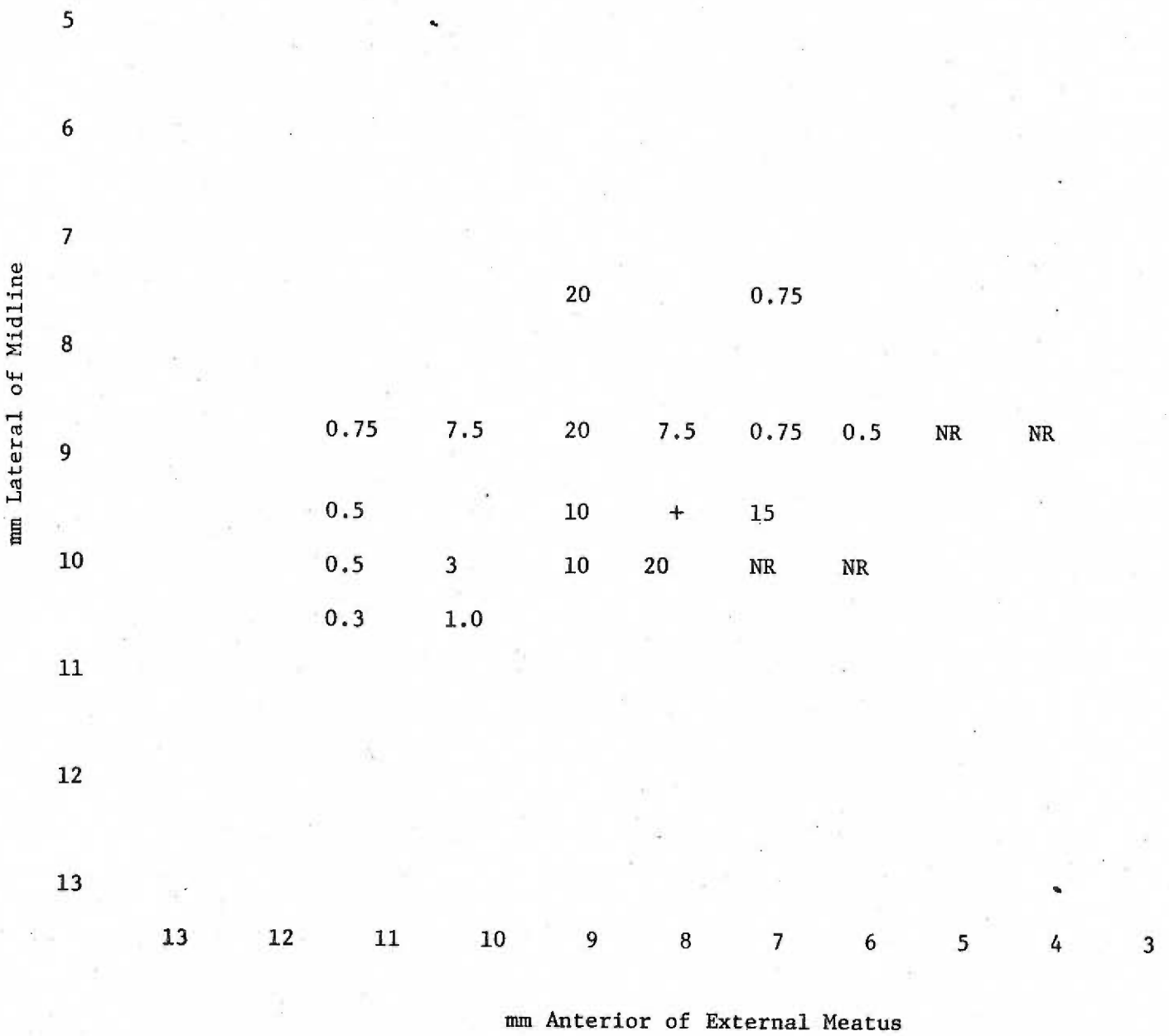
mm Lateral of Midline	13	12	11	10	9	8	7	6	5	4	3
5											
6											
7							NR				
8						7.5-30	NR				
9					2	10	10-30 +	2-10	0.300	NR	
10					2	10	10	10	NR		
11							15				
12											
13											

mm Anterior of External Meatus

Guinea Pig #91A



Guinea Pig #89A



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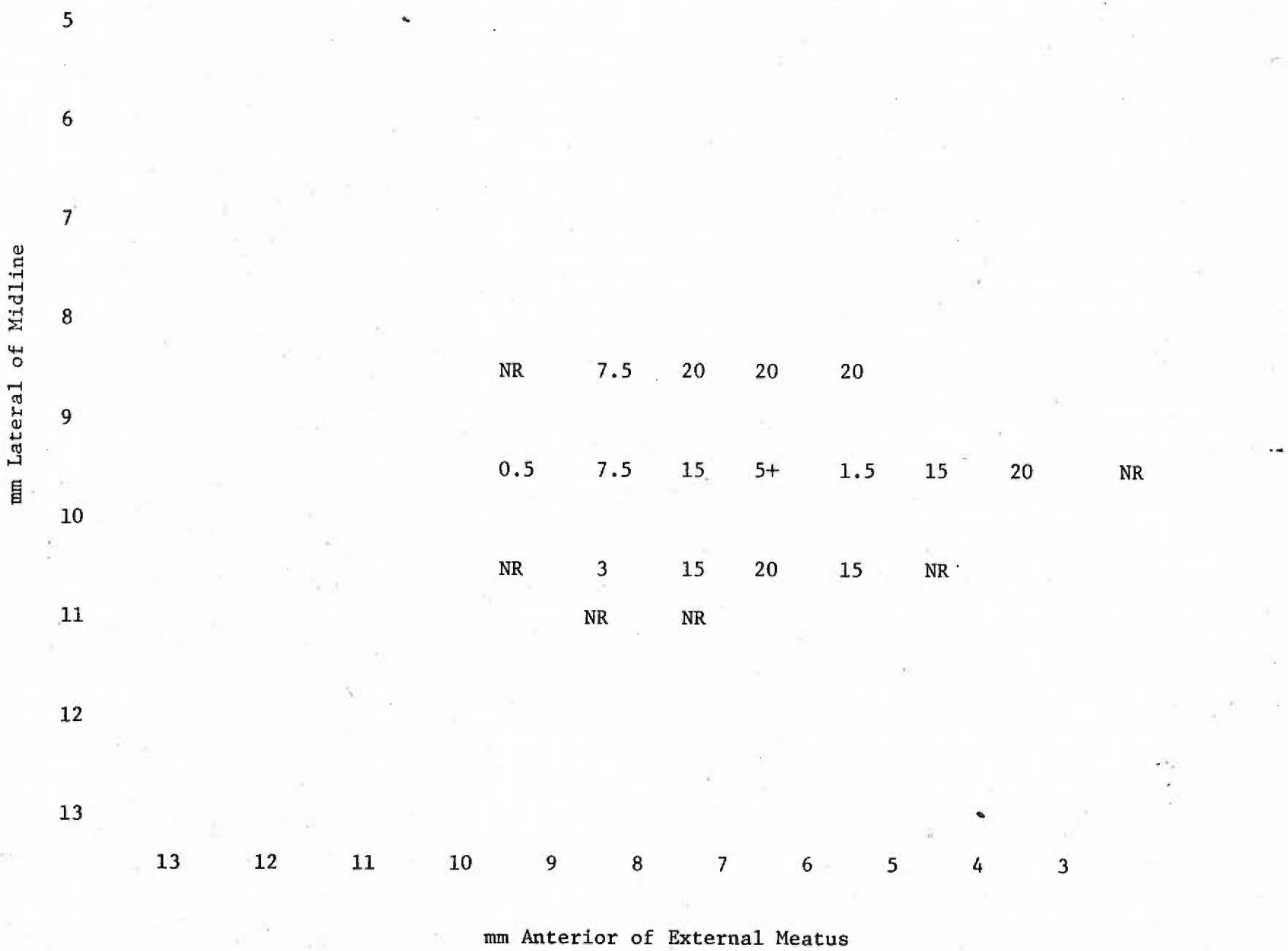

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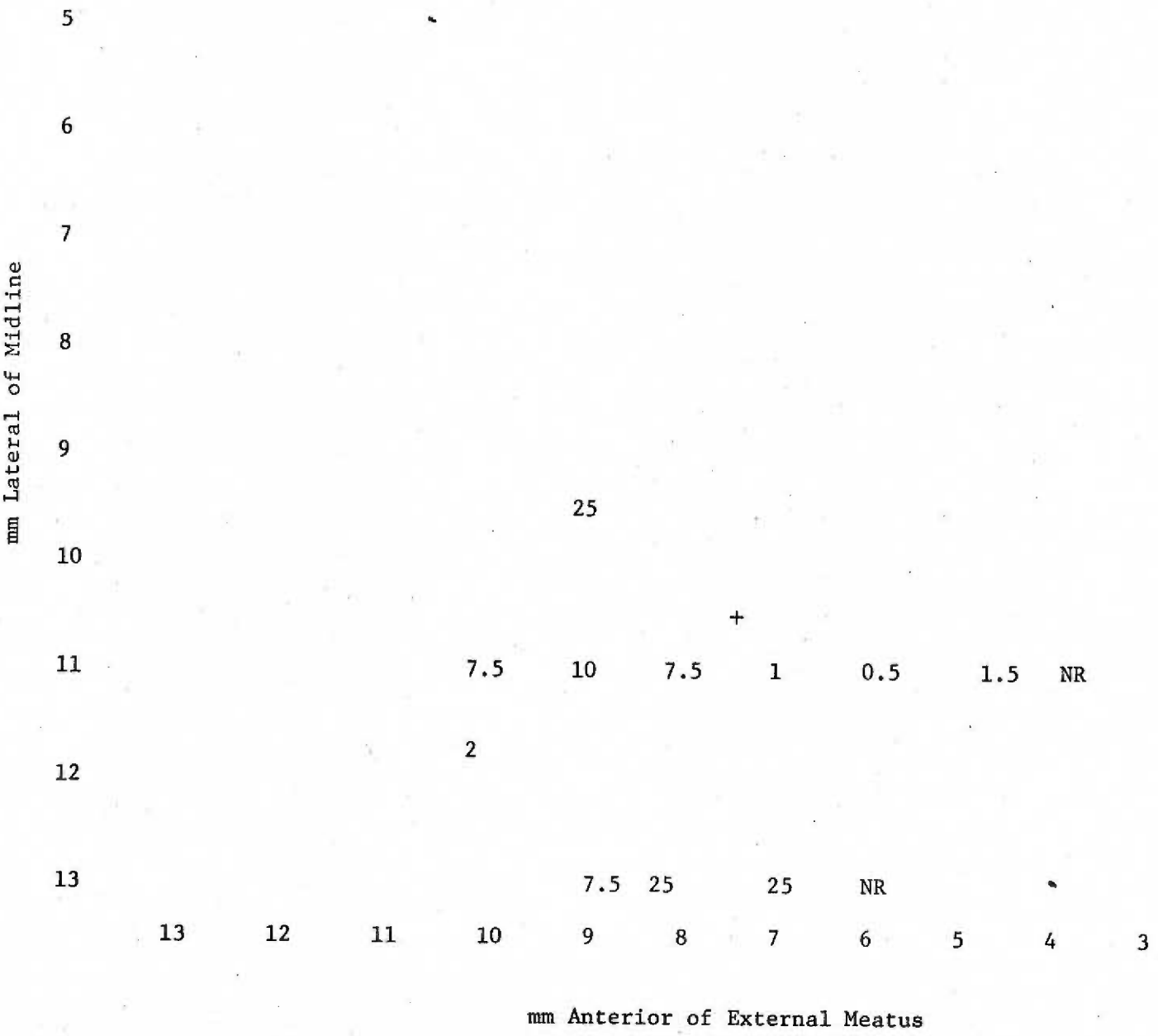
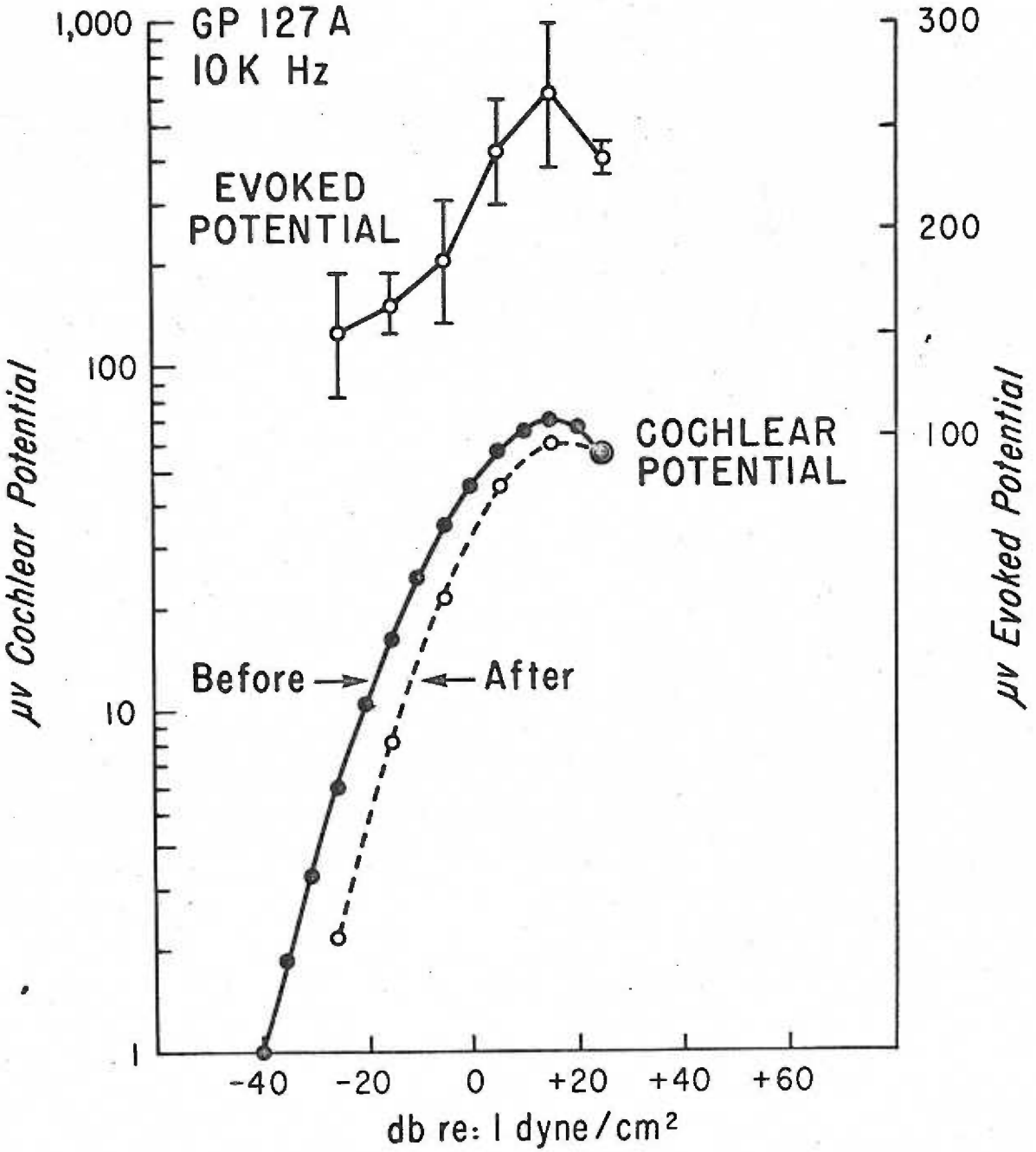
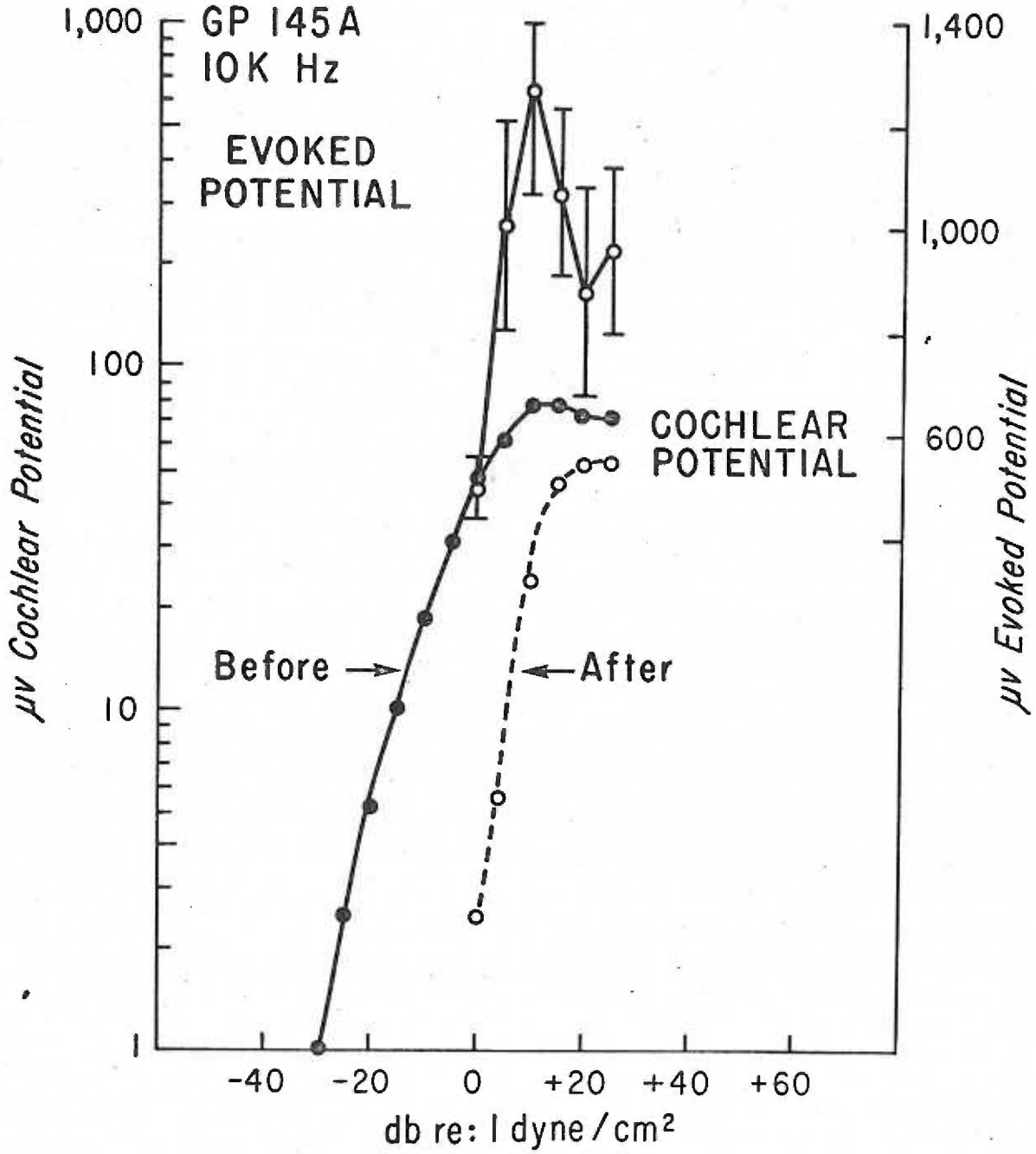
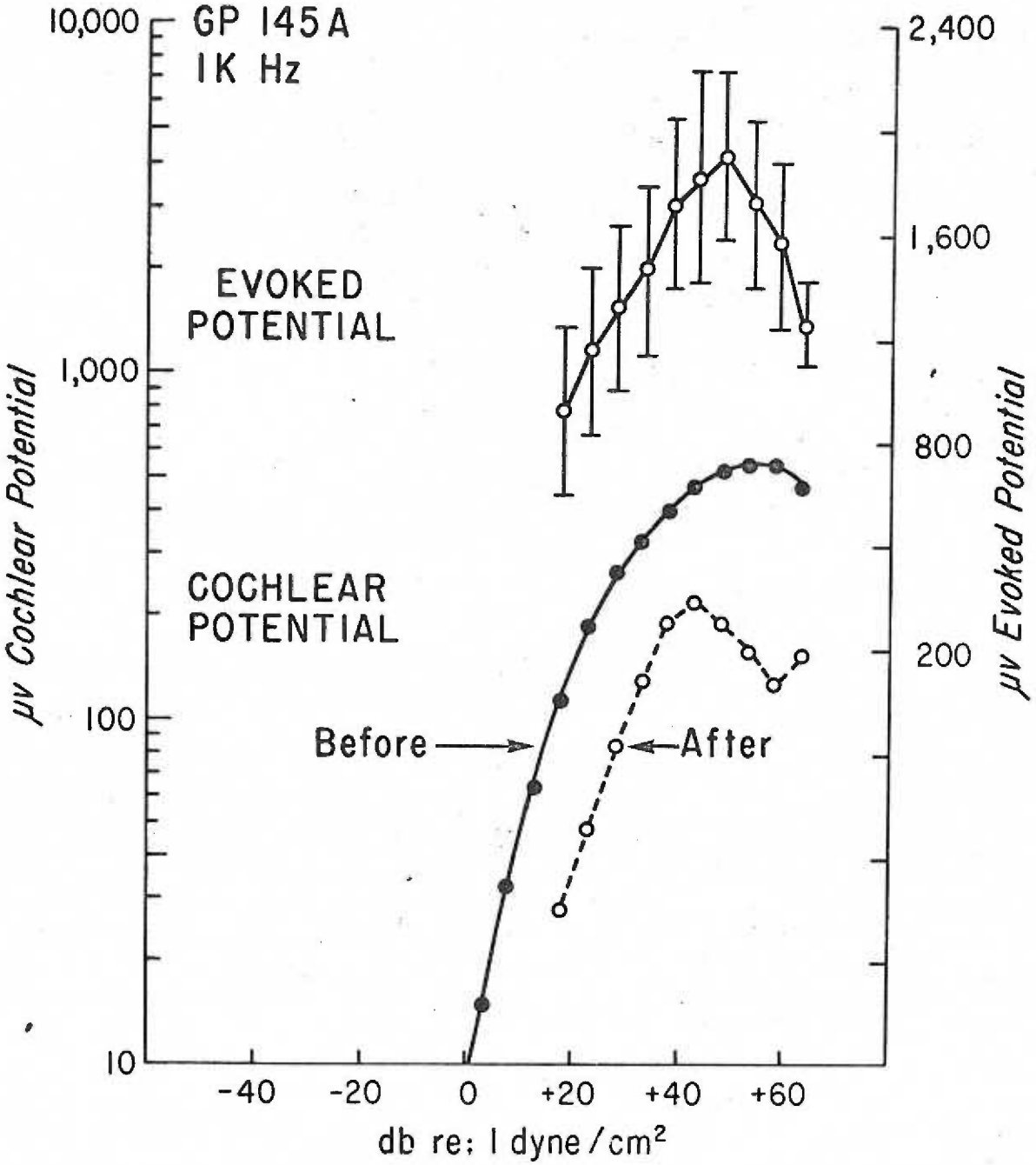


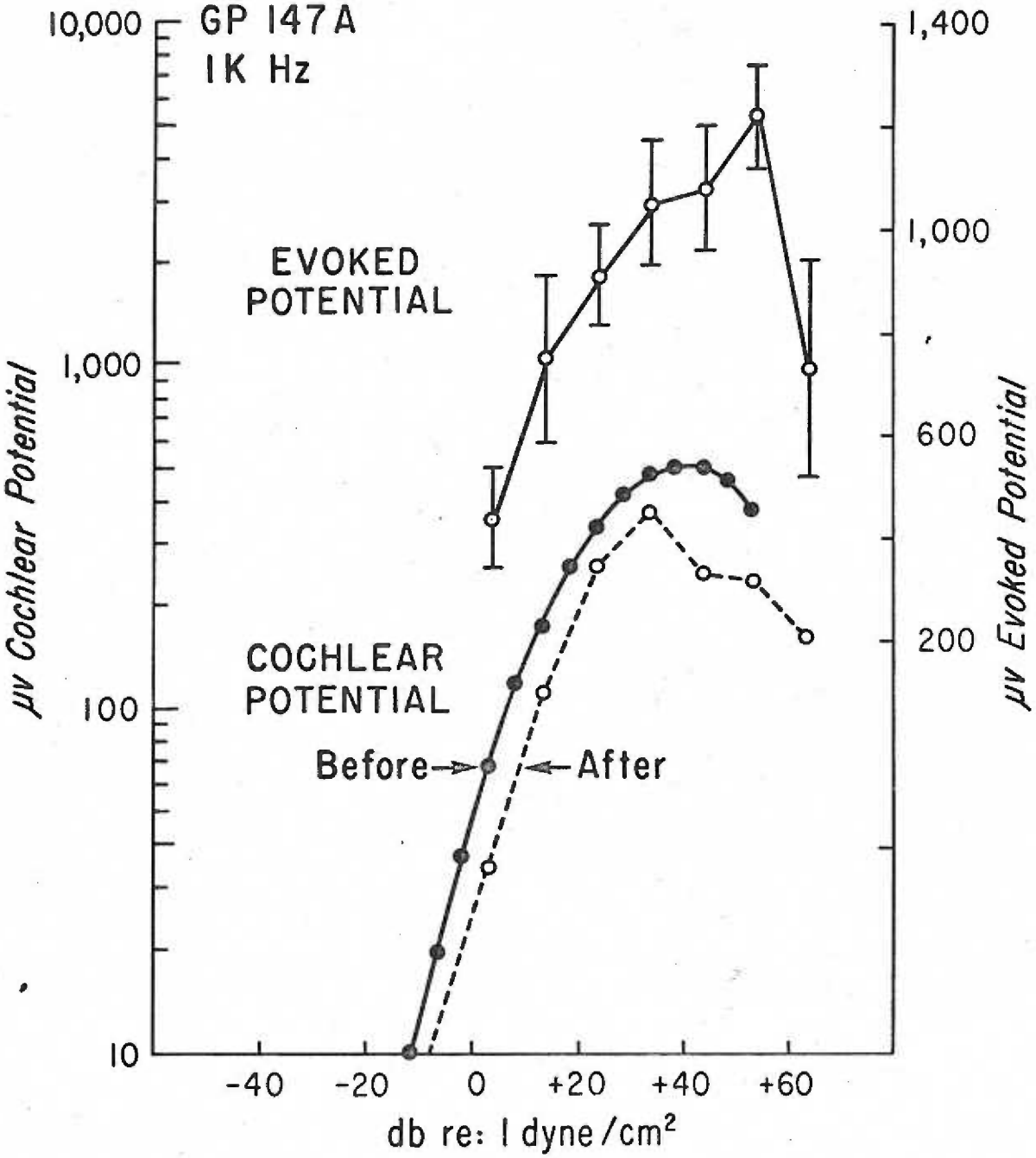
APPENDIX III

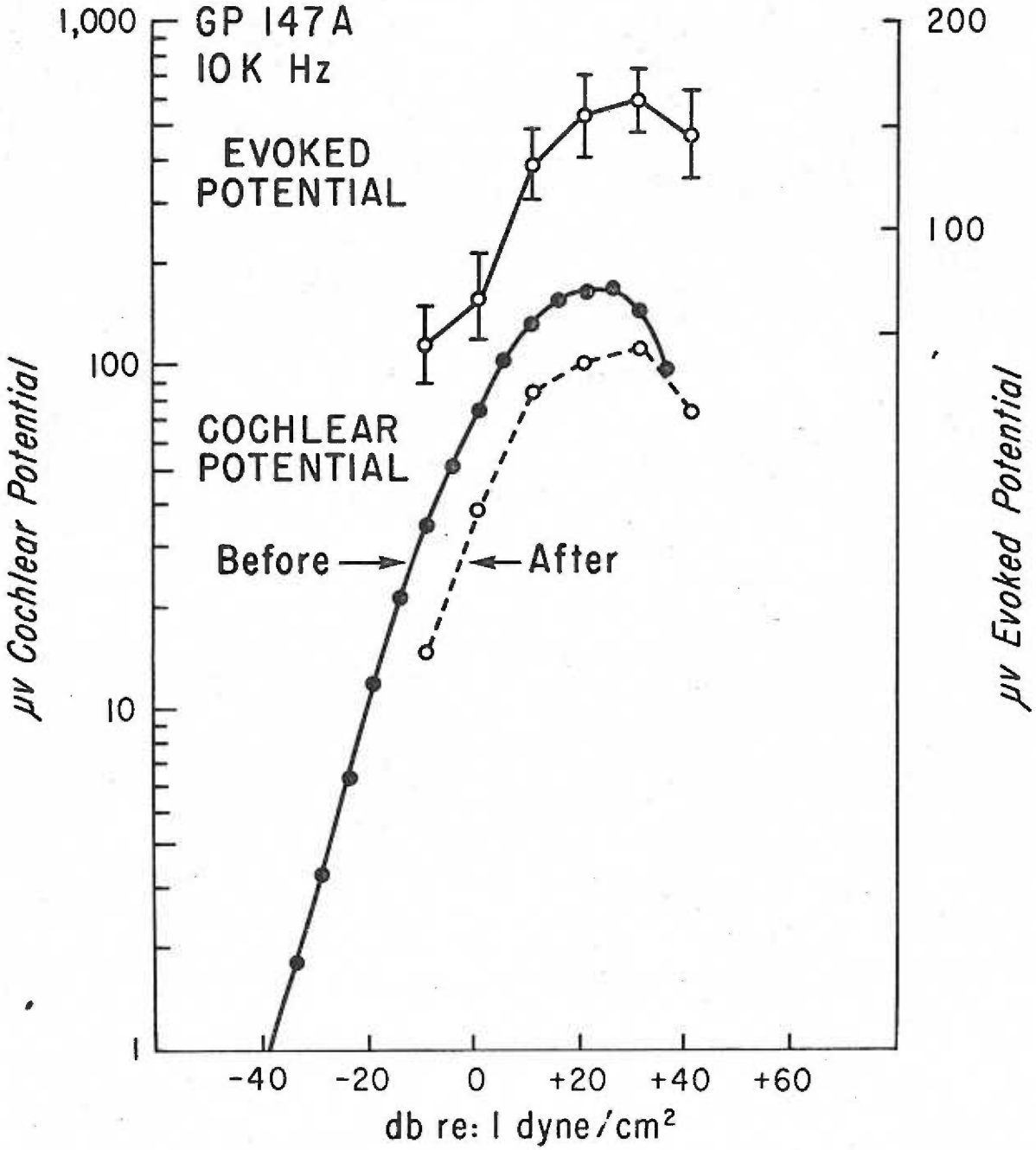
Intensity functions obtained from individual guinea pigs. Two intensity functions of the cochlear potential are shown. One of these intensity functions was obtained before the cortical intensity function was obtained. To check for possible acoustic trauma, a second intensity function of the cochlear potential was obtained after the evoked potential.

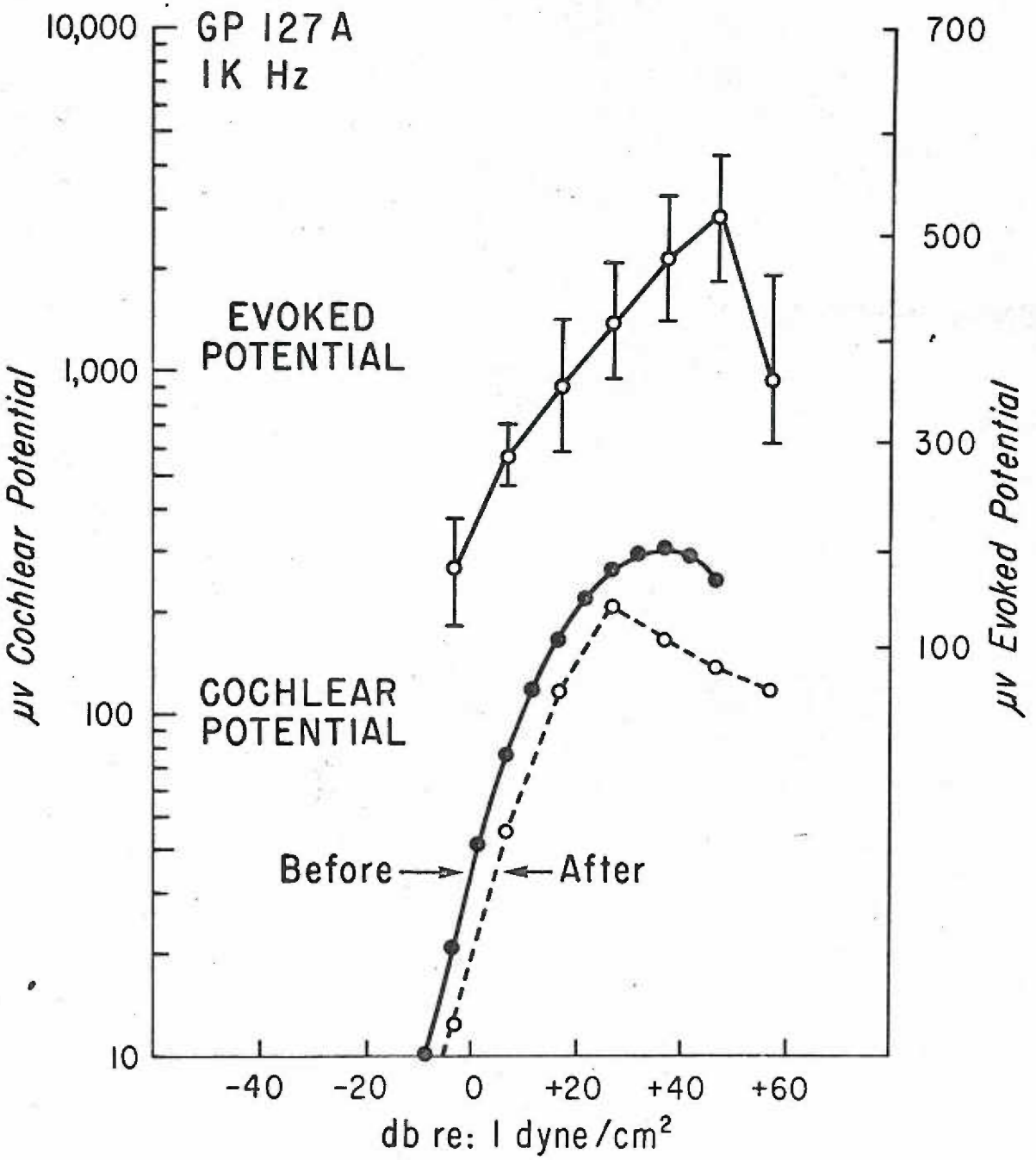

GP 127A
10K Hz
EVOKED
POTENTIAL
COCHLEAR
POTENTIAL
Before
After
1,000
100
10
1
300
200
100
-40
-20
0
+20
+40
+60
db re: 1 dyne/cm²
μv Cochlear Potential
μv Evoked Potential

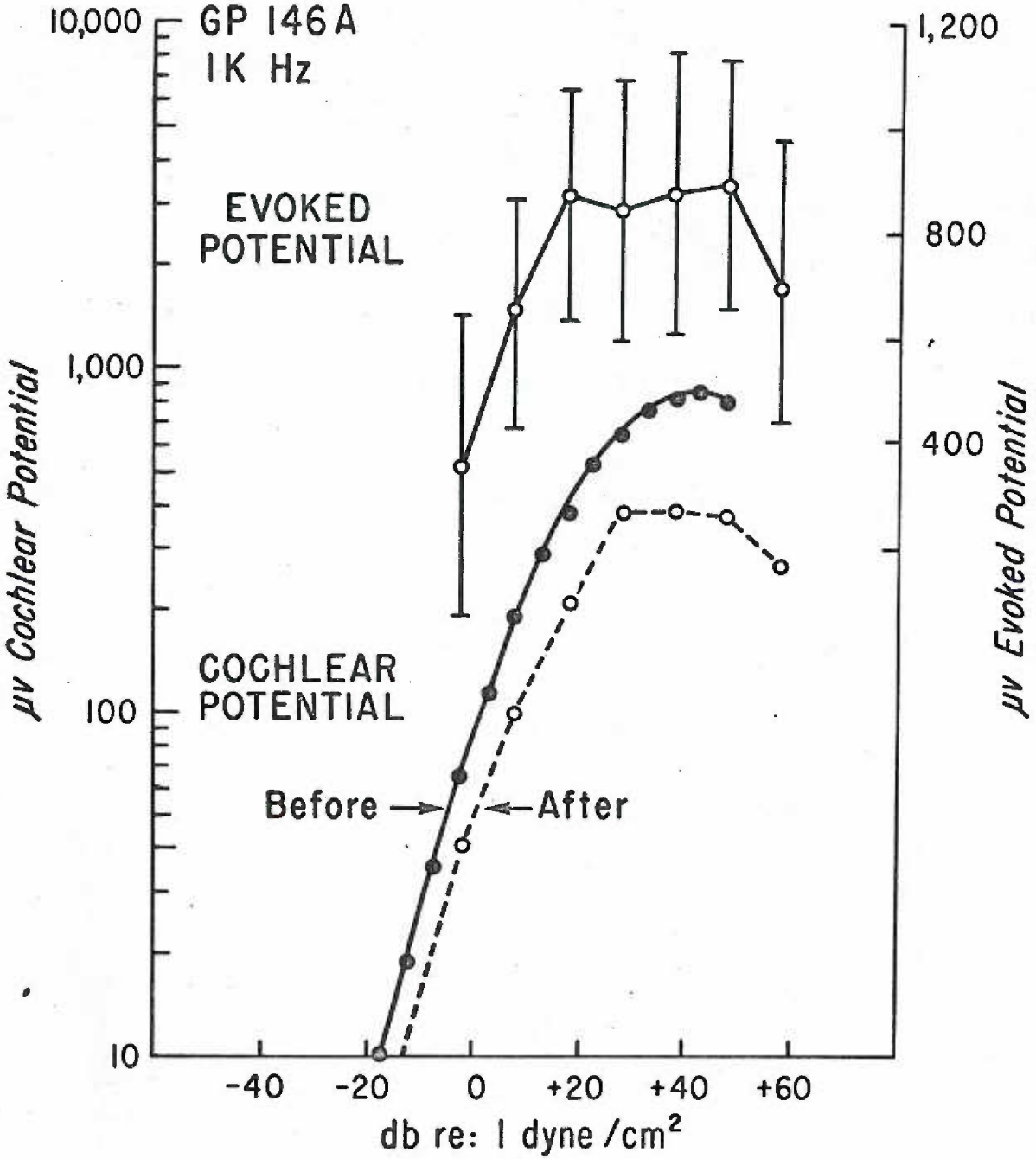

GP 145A
10K Hz
EVOKED
POTENTIAL
COCHLEAR
POTENTIAL
Before
After
1,000
100
10
1
1,400
1,000
600
μv Cochlear Potential
μv Evoked Potential
-40
-20
0
+20
+40
+60
db re: 1 dyne/cm²


GP 145A
1K Hz
EVOKED
POTENTIAL
COCHLEAR
POTENTIAL
Before
After
10,000
1,000
100
10
2,400
1,600
800
200
μv Cochlear Potential
μv Evoked Potential
-40
-20
0
+20
+40
+60
db re: 1 dyne/cm²


GP 147A
1K Hz
EVOKED
POTENTIAL
COCHLEAR
POTENTIAL
Before
After
10,000
1,000
100
10
1,400
1,000
600
200
-40
-20
0
+20
+40
+60
db re: 1 dyne/cm²
μv Cochlear Potential
μv Evoked Potential


GP 147A
10K Hz
EVOKED POTENTIAL
COCHLEAR POTENTIAL
Before
After
1,000
100
10
1
200
100
-40
-20
0
+20
+40
+60
db re: 1 dyne/cm²
μv Cochlear Potential
μv Evoked Potential


GP 127A
1K Hz
EVOKED
POTENTIAL
COCHLEAR
POTENTIAL
Before
After
10,000
1,000
100
10
700
500
300
100
-40
-20
0
+20
+40
+60
μv Cochlear Potential
μv Evoked Potential
db re: 1 dyne/cm²


GP 146A
1K Hz
EVOKED
POTENTIAL
COCHLEAR
POTENTIAL
Before
After
10,000
1,000
100
10
1,200
800
400
μv Cochlear Potential
μv Evoked Potential
-40
-20
0
+20
+40
+60
db re: 1 dyne /cm²

APPENDIX IV

Data from individual intensity runs. The numbers indicate peak to peak amplitude in microvolts. CP_b and CP_a refer to the amplitude of the cochlear potential obtained before and after the cortical runs. The numbers are r m s amplitude in microvolts.

GP 142A(10K Hz)

SOUND INTENSITY

TRIALS	-8	-3	+2	+7	+12	+17	+22	+27	+32	+37
1	500	500	680	660	860	840	520	520	640	840
2	420	540	760	840	740	860	600	340	600	700
3	380	560	640	780	440	1040	500	500	240	760
4	400	520	720	720	520	820	520	380	260	800
5	380	480	680	920	1120	960	720	400	420	900
6	440	640	820	900	820	900	600	380	460	680
7	380	440	720	1000	760	960	680	520	460	520
8	420	520	640	900	900	960	800	460	340	560
9	480	500	880	860	760	980	820	380	400	980
10	420	480	740	860	840	660	640	440	680	740
$\bar{X}$	422	518	728	844	776	898	620	432	450	748
CP_b	22	29	39	64	100	140	170	195	195	165
CP_a	5	11	25	49	82	120	160	180	185	160

GP 127A(1K Hz)

SOUND INTENSITY

TRIALS	+3	+13	+23	+33	+43	+53	+63
1	250	300	490	370	580	420	400
2	180	310	270	500	490	560	280
3	140	310	330	490	500	570	670
4	190	320	350	460	500	590	430
5	230	290	500	400	500	530	270
6	330	300	360	390	450	520	450
7	180	290	430	330	460	370	280
8	70	260	380	350	540	640	300
9	200	320	370	520	550	590	300
10	190	320	410	480	520	490	380
11	140	200	320	470	360	510	330
12	210	260	340	430	500	530	350
13	140	280	280	430	450	470	300
14	140	280	400	430	480	560	290
15	180	280	360	400	430	510	390
16	200	290	330	400	510	500	460
17	170	250	340	320	490	510	340
18	110	260	240	430	330	500	220
19	150	310	310	330	430	470	470
20	180	280	370	410	480	500	420
$\bar{X}$	179	286	359	417	478	517	362
CP_b	21	77	169	270	310	250	---
CP_a	12.	46	120	210	170	140	120

GP 147A(1K Hz)

SOUND INTENSITY

TRIALS	+4	+14	+24	+34	+44	+54	+64
1	340	620	800	960	1280	1260	600
2	280	700	780	860	1040	1100	560
3	500	680	780	980	1040	1120	680
4	440	680	720	940	840	1240	460
5	460	700	780	940	1040	1280	600
6	660	800	960	1040	1240	1360	1000
7	580	740	960	1180	1260	1380	560
8	460	780	960	980	1240	1360	1020
9	400	840	880	1180	1140	1380	580
10	380	820	900	1180	1320	1340	560
11	420	840	960	1100	1220	1320	560
12	380	720	940	1060	1240	1360	600
13	520	720	920	1000	1400	1080	520
14	360	1360	920	900	1140	1220	720
15	340	680	960	920	1140	1340	760
16	500	720	940	1180	1120	1240	1180
17	320	740	960	1100	1160	1380	1060
18	340	720	880	1040	1260	1400	960
19	520	600	1060	1140	1140	1280	900
20	580	1580	1120	1360	1420	1460	780
$\bar{X}$	439	752	909	1052	1184	1295	733
CP_b	69	175	340	490	510	380	---
CP_a	35	110	260	380	250	235	---

GP 142A(1K Hz)

SOUND INTENSITY

TRIALS	+6	+11	+16	+21	+26	+31	+36	+41	+40	+51
1	200	240	320	380	460	420	600	520	540	780
2	180	220	320	400	440	500	620	480	380	580
3	180	220	320	360	440	440	520	600	760	740
4	180	200	380	320	500	540	760	620	600	640
5	260	240	380	460	600	320	640	520	720	680
6	320	240	380	520	620	620	720	540	620	700
7	200	220	340	400	560	560	400	600	740	700
8	160	220	420	560	520	540	800	580	720	300
9	120	260	420	660	680	600	780	740	940	760
10	240	220	460	540	540	620	900	440	760	700
$\bar{X}$	204	228	374	460	536	516	674	564	678	660
CP_b	320	480	610	760	920	1050	1150	1200	1150	990
CP_a	280	380	480	610	760	940	1025	1050	1100	1000

GP 147A(10K Hz)

SOUND INTENSITY

TRIALS	-9	+1	+11	+21	+31	+41
1	35	115	155	180	165	150
2	NR	80	145	180	185	120
3	55	95	130	170	175	145
4	50	75	110	145	180	110
5	50	50	130	165	170	175
6	40	60	115	165	170	145
7	35	55	125	165	165	170
8	55	80	170	175	150	120
9	50	85	125	130	140	130
10	60	55	140	155	180	150
11	50	30	120	170	155	125
12	NR	65	160	150	175	165
13	75	60	135	130	140	185
14	40	90	130	160	185	150
15	50	45	120	175	150	160
16	50	55	130	125	170	135
17	45	60	135	150	160	170
18	45	65	135	125	165	155
19	60	45	100	150	140	135
20	50	50	130	150	150	120
$\bar{X}$	45	67	132	156	164	146
CP_b	35	76	135	165	150	100*
CP_a	45	67	86	105	115	74

*at ++36 db

GP 127A(10K Hz)

SOUND INTENSITY

TRIALS	-22	-12	-2	+8	+18	+28
1	175	160	175	220	180	315
2	145	165	265	245	285	230
3	220	140	205	225	275	255
4	170	145	175	285	275	220
5	125	145	165	215	250	190
6	220	180	170	225	290	190
7	135	180	170	280	240	170
8	150	170	180	225	275	250
9	125	160	200	210	285	265
10	175	140	160	220	280	205
11	115	185	130	280	225	200
12	145	155	160	210	295	265
13	130	155	210	250	260	230
14	140	175	195	255	205	285
15	130	170	180	230	225	255
16	155	170	165	220	230	290
17	145	165	200	260	300	205
18	140	150	160	235	290	205
19	145	150	195	240	310	215
20	150	170	220	225	300	230
$\bar{X}$	153	164	186	239	266	235
CP_b	6	17	35	58	71	57
CP_a	2	8	22	46	61	58

GP 131A(1K Hz)

SOUND INTENSITY

TRIALS	+22	+27	+32	+37	+42	+47	+52	+57
1	1250	1200	1200	1300	1500	1600	1450	1400
2	1050	1150	1350	1350	1350	1550	1350	1550
3	1050	1200	1250	1400	1500	1400	1650	1200
4	950	1150	1100	1300	1450	1550	1550	1400
5	750	1300	1150	1250	1550	1500	1500	1400
6	900	950	1250	1500	1600	1550	1750	1250
7	1250	1350	1450	1550	1650	1500	2000	1650
8	1050	1050	1450	1650	1600	1900	1900	1600
9	1250	1200	1450	1500	1650	1800	2150	1500
10	1200	1300	950	1500	1600	2000	2050	1800
$\bar{X}$	1070	1185	1260	1430	1545	1635	1735	1480
CP_b	120	180	235	275	290	300	290	265
CP_a	118	185	245	280	310	275	290	275

GP 131A(10K Hz)

SOUND INTENSITY

TRIALS	-22	-17	-12	-7	-2	+3	+8	+13	+18	+23
1	360	440	540	480	540	640	600	580	560	360
2	280	400	520	600	600	640	680	600	620	400
3	280	400	440	580	560	700	680	680	520	540
4	280	360	460	500	600	660	620	580	660	420
5	300	400	560	520	660	600	700	640	480	700
6	280	440	420	600	620	720	640	640	540	300
7	320	520	500	580	480	700	580	680	520	660
8	300	420	580	660	640	700	800	740	700	560
9	280	480	480	560	500	700	740	740	680	740
10	300	380	580	600	620	740	680	680	620	460
$\bar{x}$	298	424	508	568	582	680	672	656	590	514
CP_b	13	23	34	47	63	80	91	95	100	95
CP_a	8	14	23	35	52	69	83	93	95	87

GP 140A (10K Hz)

SOUND INTENSITY

TRIALS	-16	-11	-6	-1	+4	+9	14	19	24	29
1	460	920	660	660	840	960	880	740	640	840
2	500	680	840	820	920	920	920	900	720	700
3	440	640	720	960	740	1000	900	1020	880	920
4	760	520	660	740	1020	920	920	700	860	620
5	680	620	940	840	1060	1080	1000	1120	560	700
6	340	660	800	1120	920	780	1020	900	740	820
7	700	640	680	880	1140	2260	980	1140	1020	760
8	620	1040	1040	1280	1020	860	880	1100	860	1040
9	540	780	740	1260	1360	1260	1080	1040	1560	780
10	680	1100	1080	1480	600	1300	1520	940	1020	1300
$\bar{X}$	572	760	816	1004	962	1134	1010	960	886	848
CP_b	16	26	39	55	70	83	89	92	92	84
CP_a	12	21	32	49	65	79	87	91	89	83

GP 145A(1K Hz)

SOUND INTENSITY

TRIALS	+5	+10	+15	+20	+25	+30	+35	+40	+45	+50
1	2400	2400	2600	2900	3300	3300	3800	1450	1600	1100
2	750	1100	1100	1200	1450	1500	1600	1300	1250	1150
3	750	1050	1200	1350	1550	1700	1850	1600	1300	1250
4	900	1100	1150	1300	1550	1650	1650	1650	1450	1050
5	650	1000	1200	1250	1700	1850	1900	1900	1600	1350
6	950	1100	1500	1450	1600	1650	1650	1600	1350	1200
7	750	1000	1200	1400	1550	1550	1750	1800	1350	1250
8	900	1000	1150	900	1550	1700	1650	1700	1450	1200
9	800	1100	1200	1350	1550	1800	1750	1750	1550	1200
10	650	1050	1200	1250	1550	1700	1800	1500	1450	1150
11	1050	1000	1250	1350	1650	1550	1750	1800	1700	1350
12	900	1100	1350	1500	1650	1650	1650	1700	1550	1100
13	700	950	1150	1400	1550	1650	1700	1750	1450	1400
14	1000	1150	1450	1450	1700	1950	1950	1950	1550	1200
15	900	1150	1300	1550	1800	2000	1950	1800	1650	1400
16	850	1200	1400	1700	2000	1900	1950	2000	1650	1300
17	950	1000	1300	1400	1550	1650	2100	1850	1950	1400
18	950	1200	1400	1350	1800	1850	1900	1650	1600	1350
19	900	1300	1450	1700	1750	1950	1650	1750	1700	1300
20	1000	1250	1200	1800	1800	1950	2150	2000	2100	1500
$\bar{X}$	935	1160	1338	1475	1725	1825	1908	1725	1567	1260
CP_b	64	115	185	260	320	400	470	520	540	540*
CP_a	28	48	82	130	190	220	190	160	125	155

* 490 uv at +53 db

GP 145A(10K Hz)

SOUND INTENSITY

TRIALS	0	+10	+20	+30	+35	+40
1	700	950	1450	1050	850	1000
2	750	1350	950	750	1000	1250
3	450	1250	1050	1550	500	700
4	450	1000	1400	950	850	1050
5	600	900	1400	1400	900	1100
6	400	900	1450	1000	1100	850
7	550	900	1550	900	700	850
8	400	800	1400	1450	1000	850
9	500	1350	850	1200	900	850
10	500	900	1450	1100	700	1000
11	450	1000	850	950	500	1100
12	550	950	1150	1200	1050	950
13	300	700	1250	1050	950	1000
14	400	850	1100	1250	850	900
15	350	900	950	850	850	750
16	400	650	1350	1100	700	750
17	700	1100	1600	1100	1400	1350
18	650	1500	1450	850	1100	1250
19	400	1350	1450	800	850	750
$\bar{X}$	500	1015	1268	1078	881	963
CP_b	20	54	80	90	78	---
CP_a	3	6	24	46	52	52

GP 146A(1K Hz)

SOUND INTENSITY

TRIALS	-2	+8	+18	+28	+38	+48	+58
1	280	660	680	1020	740	540	240
2	280	580	660	680	380	760	300
3	140	580	600	960	1040	720	760
4	200	420	820	720	880	1040	800
5	540	580	700	320	980	800	620
6	140	780	820	600	200	980	540
7	320	620	1000	580	880	500	720
8	800	460	760	820	660	820	900
9	220	980	860	800	1180	700	420
10	280	160	940	880	1160	720	1080
11	360	360	1140	940	1040	700	1080
12	280	800	1200	660	1060	1200	360
13	360	1040	760	1060	640	1220	580
14	320	620	860	1040	1080	1160	820
15	620	960	980	820	740	1180	920
16	240	940	1280	880	1060	900	260
17	540	520	1060	1060	1140	1280	700
18	320	880	660	460	800	600	300
19	240	740	460	1300	640	900	760
20	500	480	1180	1200	1180	1140	780
$\bar{X}$	349	658	871	840	874	893	647
CP_b	65	190	380	650	830	820	---
CP_a	41	100	205	390	390	380	270

GP 146A(10K Hz)

SOUND INTENSITY

TRIALS	-22	-12	-2	+8	+18	+28
1	480	510	600	410	770	720
2	300	560	640	670	730	500
3	450	530	570	740	760	690
4	400	540	590	710	790	530
5	730	500	740	760	770	570
6	490	520	690	720	770	770
7	540	560	650	730	620	780
8	240	480	730	750	700	520
9	330	500	740	700	760	550
10	550	550	570	670	820	670
11	540	320	640	780	730	510
12	360	530	720	760	800	710
13	590	420	700	650	660	590
14	390	550	640	640	540	560
15	490	590	550	770	710	770
16	470	510	680	640	690	660
17	570	630	560	690	700	480
18	450	490	570	540	700	650
19	410	430	560	670	740	570
20	410	570	600	620	730	580
$\bar{X}$	460	515	637	681	725	589
CP_b	21	62	128	195	225	220*
CP_a	15	44	94	155	189	175

*at +23 db

APPENDIX V

The response to sound for some guinea pigs that were later stimulated electrically. CP refers to the 1 uv cochlear potential sensitivity function. This was recorded from each of the two intracochlear electrodes. The other functions (such as A10 L10) refer to the threshold for an evoked cortical potential. The numbers refer to the cortical positon.

GUINEA PIG

		FREQUENCY								
		100	300	500	1K	3K	5K	10K	15K	25K
151A	CP_1	-25	-30	-39	-33	-20	-39	-35	-25	---
	CP_2	-26	-32	-42	-32	-23	-40	-35	-27	---
	A10 L10	+10	- 2	-16	-14	- 3	-27	-24	NR	---
153A	CP_1	-51	-48	-60	-38	-55	-50	-40	-40	-42
	CP_2	-54	-59	-61	-40	-53	-51	-35	-28	-46
	A8 L11	-41	-37	-39	-41	-54	-54	-57	-45	-46
	A11 L11	-33	-42	-38	-36	-55	-56	-56	-12	-32
	A8 L6	NR	NR	NR	NR	NR	NR	NR	NR	NR
154A	CP_1	-43	-45	-55	-45	-40	-32	-47	-35	+ 5
	CP_2	-41	-45	-55	-51	-50	-30	-46	-40	+ 1
	A8 L11	-10	- 6	-13	-21	-42	-39	-47	-14	+12
	A8 L6	NR	NR	NR	NR	NR	NR	NR	---	---
156A	CP_1	-28	-16	-30	-35	-47	-24	-33	-36	+ 3
	CP_2	-22	-11	-25	-31	-43	-19	-24	-24	+ 7
	A11 L12	+21	+ 9	- 6	-21	-23	-16	-23	-15	+19
	A8 L12	+16	+ 4	-11	-26	-43	-37	-43	-35	+19
	A6 L6	---	---	---	NR	---	NR	NR	---	---
159A	CP_a	-44	-49	-49	-57	-48	-20	-34	-26	- 4
	CP_b	-23	-32	-47	-46	-61	-35	-45	-28	+ 6
	A10 L11	+ 7	+24	+13	+20	- 5	+17	+10	+ 6	NR
	A8 L6	NR	NR	NR	NR	NR	NR	NR	NR	NR
172A	CP_a	-25	-34	-28	-30	-36	-14	-19	+ 1	---
	CP_b	+ 1	- 9	-17	-15	-37	-17	-39	-20	---
	A8 L8	NR	NR	+33	+25	+ 3	+13	- 9	0	---

GUINEA PIG

		FREQUENCY								
		100	300	500	1K	3K	5K	10K	15K	25K
174A	CP_a	-42	-35	-49	-27	-39	-37	-29	- 3	+31
	CP_b	-20	-39	-41	-24	-44	-36	-36	-21	+11
	A10 L8	+20	+10	+ 9	+26	+ 6	+ 8	-39	-15	+11
175A	CR_v	-17	-26	-26	-11	-21	-11	- 4	+ 2	+34
	CP_k	- 2	-11	-14	-11	-18	- 4	-10	- 1	+17
	A10 L9	NR	NR	NR	NR	NR	NR	+20	+10	NR

APPENDIX VI

Damage due to electrical stimulation. The data are 1 uv cochlear potential sensitivity functions obtained before and after thresholds for electrical stimuli were obtained.

GUINEA PIG

		FREQUENCY								
		100	300	500	1K	3K	5K	10K	15K	25K
151A	Before	-26	-32	-42	-32	-23	-40	-35	-27	-38
	After	-21	-28	-43	-29	-20	-37	-55	-19	-9
	Difference	-5	-4	+1	-3	-3	-3	+20	-6	-31
161A	Before	-59	-32	-27	-28	-48	-41	-35	-38	-9
	After	-45	-26	-16	-18	-37	-32	-17	-26	+2
	Difference	-14	-6	-11	-10	-11	-9	-18	-12	-11
172A	Before	-25	-34	-28	-30	-36	-14	-19	+1	---
Apex	After	-24	-34	-30	-28	-34	-15	-15	+1	---
	Difference	-1	0	+2	-2	-2	+1	-4	0	---
174A	Before	-42	-35	-49	-27	-39	-37	-29	-3	+31
Apex	After	-44	-46	-44	-26	-31	-39	-26	+1	+16
	Difference	+2	+11	-5	-1	-8	+2	-3	-4	+25

APPENDIX VII

Thresholds for electrically evoked potential. Both stimulating electrodes were in scala tympani of the basal turn. The recording was made either from a cortical position within the auditory area or from a position outside the auditory area.

GUINEA PIG

FREQUENCY

		100	300	500	1K	3K	5K	10K	15K	25K
153A	Auditory Area	3.2	3.8	6.3	14.1	21.1	22.1	9.1	5.7	156.9
	Non-auditory area	9.2	15.4	22.5	55.0	83.8	124.4	231.2	400.7	625.6
	Ratio	2.87	4.05	4.25	3.90	3.90	5.62	25.41	70.17	3.98
	db	- 9.1	-12.1	-12.5	-11.8	-11.8	-14.9	-28.0	-37.0	-12.0
154A	Auditory Area	2.6	6.6	10.8	18.6	39.0	16.1	7.3	127.6	179.2
	Non- " "	4.3	13.7	20.9	40.3	189.0	375.0	45.45	---	---
	Ratio	1.65	2.08	1.94	2.17	4.85	23.29	62.26	---	---
	db	- 4.3	- 6.3	- 5.7	- 6.8	-13.7	-30.3	-35.9	---	---
156A	Auditory Area	11.0	16.4	19.2	25.7	16.7	6.6	21.0	58.3	67.6
	Non- " "	19.6	36.2	47.8	61.0	93.7	118.7	133.7	---	---
	Ratio	1.78	2.21	2.49	2.37	5.61	17.98	6.37	---	---
	db	- 4.9	- 6.9	- 7.9	- 7.5	-14.9	-38.0	-16.0	---	---
159A	Auditory Area	9.6	16.0	24.0	41.5	95.0	119.0	236.0	375.0	---
	Non- " "	42.8	63.1	106.2	163.4	---	---	---	---	---
	Ratio	4.46	3.95	4.43	3.94	---	---	---	---	---
	db	-12.8	-12.0	-12.9	-11.9	---	---	---	---	---

APPENDIX VIII

Thresholds for electrically stimulating the cochlea.

* both electrodes in scala tympani of basal turn.

+ one electrode in apex, the other electrode in scala tympani of basal turn

X one electrode in scala tympani of the basal turn; the other electrode in scala vestibuli of the basal turn.

FREQUENCY

TRIALS	100	300	500	1K	3K	5K	10K	15K	25K
151A(A10 L10)*									
db	15	18	18	19	16	14	14	6	---
mv	540	390	390	360	480	600	600	1500	---
Kohms	---	---	---	---	---	---	---	---	---
uA	---	---	---	---	---	---	---	---	---
153A(A8 L11)*									
db	14	17	18	18	24	30	47	36	11
mv	600	420	380	380	189	95	14	48	846
Kohms	82	35	24	12	8	6.8	5.8	5.3	4.8
uA	7.3	12.0	15.8	31.6	23.6	13.9	2.4	9.1	176.2
153A(A11 L11)*									
db	21	27	26	25	25	20	35	40	12
mv	267	134	150	169	169	150	53	30	753
Kohms	82	35	24	12	8	6.8	5.8	5.3	4.8
uA	3.2	3.8	6.3	14.1	21.1	22.1	9.1	5.7	156.9
154A(A8 L11)*									
db	19	19	18	18	18	27	36	12	10
mv	360	360	390	390	390	134	48	753	950
Kohms	141	55	36	21	10	8.3	6.6	5.9	5.3
uA	2.6	6.6	10.8	18.6	39.0	16.1	7.3	127.6	179.2

	FREQUENCY								
TRIALS	100	300	500	1K	3K	5K	10K	15K	25K
156A(A11 L12)*									
db	-10	-15	-16	-15	-20	-28	-17	- 7	- 4
mv	950	540	480	540	300	119	420	1341	1893
Kohms	86	33	25	21	18	18	20	23	28
uA	11.0	16.4	19.2	25.7	16.7	6.6	21.0	58.3	67.6
156A(A8 L12) *									
db	-10	-12	-11	-11	-12	-23	-46	-38	-14
mv	950	753	840	846	753	212	15	38	600
Kohms	86	33	25	21	18	18	20	23	28
uA	11.0	22.8	33.6	40.3	41.8	11.7	0.7	1.7	21.5
161A(A8 L10) *									
db	14	17	12	10	9	14	33	34	9
mv	600	420	753	950	1065	600	67	36	1065
Kohms	---	15	24	9	4	2.5	1.5	1.0	0.5
uA	---	28.0	31.4	105.5	266.2	240.0	44.6	36.0	2130.0
159A(A10 L11)+									
db	13	16	16	15	10	8	3	0	NR
mv	670	480	480	540	950	1194	2124	3000	---
Kohms	70	30	20	13	10	10	9	8	6
uA	9.6	16.0	24.0	41.5	95.0	119.0	236.0	375.0	---

FREQUENCY

TRIALS	100	300	500	1K	3K	5K	10K	15K	25K
172A (A8 L8) +									
db	28	31	28	24	20	18	14	10	4
mv	119	84	119	189	300	390	600	950	1893
Kohms	---	---	---	---	---	---	---	---	---
uA	---	---	---	---	---	---	---	---	---
174A(A10 L8) +									
db	-21	-25	-23	-21	-17	-14	-17	-17	- 2
mv	267	169	212	267	420	600	420	846	2382
Kohms	66	28	19	13	715	6.5	6	5.2	4.6
uA	4.0	6.0	11.2	20.5	56.0	92.3	70.0	162.6	517.0
175A(A10 L9) X									
db	6	7	6	3	3	2	2	NR	NR
mv	1500	1341	1500	2124	2124	1893	1893	---	---
Kohms	34	19	14	9	4.6	3.4	2.4	1.9	---
uA	44.1	70.5	107.1	236.0	461.7	556.7	788.8	---	---
162A *									
db	14	16	14	14	17	15	10	6	2
mv	600	480	600	600	420	540	950	1500	1893
Kohms	---	---	---	15	7	4	2	1.5	1.4
uA	---	---	---	40.0	60.0	135.0	475.0	1000.0	1352.0

FREQUENCY

TRIALS	100	300	500	1K	3K	5K	10K	15K	25K
*									
153A(A8 L8)									
db	12	15	15	14	13	11	7	3	0
mv	753	540	540	660	670	846	1341	2124	3000
Kohms	82	35	24	12	8	6.8	5.8	5.3	4.8
uA	9.2	15.4	22.5	55.0	83.8	124.4	231.2	400.7	625
*									
156A(A8 L6)									
db	-5	-8	-8	-7	-5	-3	-1	---	---
mv	1686	1194	1194	1341	1686	2124	2673	---	---
Kohms	86	33	25	21	18	18	20	23	28
uA	19.6	36.2	47.8	61.0	93.7	118.7	133.7	---	---
*									
154A(A8 Lg)									
db	14	12	12	11	4	0	0	---	---
mv	600	753	753	846	1893	3000	3000	---	---
kohms	141	55	36	21	10	8.3	6.6	5.9	5.3
uA	413	13.7	20.9	40.3	189.0	375.0	454.5	---	---
+									
159A(A8 L6)									
db	0	4	3	3	NR	NR	NR	NR	NR
mv	3000	1893	2124	2124	---	---	---	---	---
Kohms	70	30	20	13	10	---	---	---	---
uA	42.8	63.1	106.2	163.4	---	---	---	---	---
+									
172A(A8 L5)									
db	0	0	0	NR	NR	NR	NR	NR	NR
mv	3000	3000	3000	---	---	---	---	---	---
Kohms	---	---	---	---	---	---	---	---	---
uA	---	---	---	---	---	---	---	---	---

APENDIX IX

Threshold for electrical stimulation of cochlea after acoustic trauma suppressed the cochlea's responsiveness to sound.

	FREQUENCY								
TRIALS	100	300	500	1K	3K	5K	10K	15K	25K
161A *									
db	-16	-25	-25	-22	-14	-11	-3	NR	NR
mv	480	168	168	189	600	840	2124	---	---
Kohms	---	15	24	9	4	2.5	1.5	1.0	0.5
uA	---	11.2	4.5	21.0	150.0	336.0	1416.0	---	---
162A *									
db	13	16	13	11	8	6	5	2	NR
mv	670	480	670	846	1194	1500	1686	1893	---
Kohms	---	---	---	15	7	4	2	1.5	1.4
uA	---	---	---	56.4	170.6	375.0	843.0	1262.0	---